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## RESPIRATORY AND PUPILLARY REACTIONS

INDUCED BY ELECTRICAL STIMULATION OF THE  
HYPOTHALAMUS

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It is generally recognized that the hypothalamus contains centers regulating autonomic activity. Experimental evidence which points to this conclusion has been obtained as a result of gross lesions or extirpation of this region, or by the injection of chemicals into the base of the brain. Karplus and Kreidl<sup>1</sup> (1910) have supplied further data by making transverse ablations through the diencephalon and stimulating the exposed end. Never before has a systematic exploration of the intact hypothalamus with electrical stimulation been undertaken. The foundation for such an investigation has been laid by the accurate anatomic studies of Rioch<sup>2</sup> (1929, 1931).

Using the Horsley-Clarke instrument and a bipolar needle electrode, we have explored the hypothalamic region millimeter by millimeter in each of twenty-two cats. These animals were observed for changes in the pupil, in the respiratory rate, in temperature and in the rate of urinary flow. They were watched also for any signs of erection of the hair and for any increase in the flow of saliva. The results obtained serve to localize certain of these functions with a degree of accuracy that has not hitherto been achieved.

### METHOD

The animals were given intraperitoneal injections of a small dose of pentobarbital sodium, 18 mg. per kilogram of body weight. A tracheal cannula was

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From the Institute of Neurology, Northwestern University Medical School.  
Read at the Chicago Neurological Society, Chicago, Oct. 20, 1932.

1. Karplus, J. P., and Kreidl, A.: *Gehirn und Sympathicus*: II. Ein Sympathicus Zentrum im Zwischenhirn, *Arch. f. d. ges. Physiol.* **135**:401, 1910.

2. Rioch, D. McK.: Studies on the Diencephalon of Carnivora: I. The Nuclear Configuration of the Thalamus, Epithalamus, and Hypothalamus of the Dog and Cat, *J. Comp. Neurol.* **49**:1, 1929; II. Certain Nuclear Configurations and Fiber Connections of the Subthalamus and Midbrain of the Dog and Cat, *ibid.* **49**:121, 1929; III. Certain Myelinated-Fiber Connections of the Diencephalon of the Dog, Cat, and Avisa, *ibid.* **53**:319, 1931.

then introduced and light anesthesia maintained by the use of an ether bottle. A small incision was made in the lower abdominal wall in order to catheterize the bladder through a slit in the urethra.

The calvarium was exposed and a square of about one-half inch (1.3 cm.) removed. The superior sagittal sinus was then tied off and the dura removed. Following this, the Horsley-Clarke instrument was adjusted to the animal's head, and the electrode was inserted into the brain. The instrument and the manner in which it is used has been described in a paper by Ingram, Ranson, Hannett, Zeiss and Terwilliger<sup>3</sup> (1932). With this apparatus it is possible to stimulate one point after another in the interior of the brain, always being aware of the location of each point stimulated with reference to the others and also with reference to a fixed zero point. This point is located at the intersection of the interaural frontal plane and the midsagittal plane at a distance above the meatus of from 10 to 11 mm., depending on the size of the cat. The coordinates of each point stimulated are recorded in terms of millimeters to the right or left, above or below and in front of or behind this point.

The bipolar electrode consisted of two lengths of enameled nichrome wire cemented together with chlorinated rubber. Its diameter through the widest axis was 0.8 mm.; the shortest distance between the tips was 0.2 mm. The primary current of 1.5 amperes, furnished by one dry cell, passed through a Harvard inductorium, the secondary coil of which was set at 9 cm.

The electrode was inserted vertically into the rostral part of the diencephalon at a point 1 mm. to the left of the midline and 11, 12 or 13 mm. in front of the interaural plane. The electrode was pushed down a few millimeters at a time in order that stimuli might be applied at various points along its course. The points stimulated along each puncture were at +4, +2, 0, -2, -3, -4, -5 and -6, where zero indicated the zero horizontal plane of the instrument and + indicated the millimeters above and - the millimeters below that plane. Stimuli at +4, +2 and 0 were in the dorsal thalamus, and the remaining points in the subthalamus and hypothalamus. When the stimuli along the first line of puncture had been completed, the electrode was withdrawn from the brain and moved to a position 1 mm. to the right of the midline and lowered again in the manner just described. In a similar way stimulation was applied along punctures 2, 3, 4, 5 and 6 mm. to the right of the midline. On conclusion of such a row of punctures, all in the same transverse plane, the electrode was moved 2 mm. further caudal, and another row from left to right was completed as before. From three to five of these transverse rows were made in each cat. Since in some experiments these rows were in planes 13, 11, 9 and 7 mm., and in others 12, 10, 8 and 6 mm., in front of the interaural plane, the hypothalamus was thoroughly explored and sometimes the last plane of stimulation lay in the rostral portion of the midbrain.

In each experiment about two hundred separate points were stimulated. An accurate record was kept of the coordinates of these points and of the responses obtained from each. Since the thalamus is almost entirely silent, the negative results obtained from it served as a control for the observations on the hypothalamus. When a marked and characteristic reaction was obtained, the puncture was not continued beyond that point in order that the locus might be more accurately identified in microscopic sections of the brain.

At the conclusion of the experiment the head was given an injection of formaldehyde, and the brain was removed and prepared for microscopic study by the Weil

3. Ingram, W. R.; Ranson, S. W.; Hannett, F. I.; Zeiss, F. R., and Terwilliger, E. H.: Results of Stimulation of the Tegmentum with the Horsley-Clarke Stereotaxic Apparatus, *Arch. Neurol. & Psychiat.* **28**:513 (Sept.) 1932.

method. The level of the sections was identified and the reactions were plotted on a series of standard drawings of the hypothalamus made by Dr. F. I. Hannett in this laboratory. Calculations were made for shrinkage of the sections, and the points of stimulation were determined along the fine tracks of hemorrhage which marked the path of the electrode by measuring upward from the end of the puncture. These calculations could be checked by comparison with the position of the points which had been definitely marked by stopping certain of the punctures when an especially marked reaction was obtained. These locations could be readily identified at the ends of the punctures, and their exact coordinates were known.

#### RESULTS

As has been indicated, stimuli in the thalamus were made on all of the punctures. This procedure was followed as a control measure. No reactions were obtained from the thalamus except that stimuli in the reticular nucleus, in the most rostral part of the thalamus, produced an inhibition of respiration. Sachs<sup>4</sup> (1911) obtained a similar result from the anterior nucleus and some other parts of the thalamus. These negative results serve to emphasize the data to follow, obtained from the same series of animals, under the same conditions, but from stimulation of the hypothalamus.

Obviously, brief stimuli applied to one point after another in rapid succession can give information concerning the localization of only those functions in which rapid alterations are detectable, such as diameter of the pupil and rate of respiration. Observations on the flow of urine and saliva and on temperature were made, however, in order that any effects which might be produced by the sum of the stimuli at a given level should be registered.

A marked increase in the flow of urine during stimulation was observed in only two of the twelve cats in which detailed records of urinary flow were kept. In both of these cats the rate of flow under experimental conditions, but before stimulation was begun, was 1 cc. of urine in thirty minutes. During stimulation the rate increased to 4 cc. of urine in thirty minutes. The level of stimulation was in one case through the mammillary bodies and in the other included the region from the mammillary bodies to the third nerve. The two positive cases are of questionable significance in view of the fact that ten cats showed no increase at these or any other levels.

No apparent increase in the flow of saliva was manifested during any of the experiments, but for an accurate study of this cannulation of the salivary ducts would be necessary. Erection of hair never occurred. These animals were under pentobarbital sodium anesthesia, and the possibility that this may have depressed autonomic responses must be

4. Sachs, E.: On the Relation of the Optic Thalamus to Respiration, Circulation, Temperature and the Spleen, *J. Exper. Med.* **14**:408, 1911.

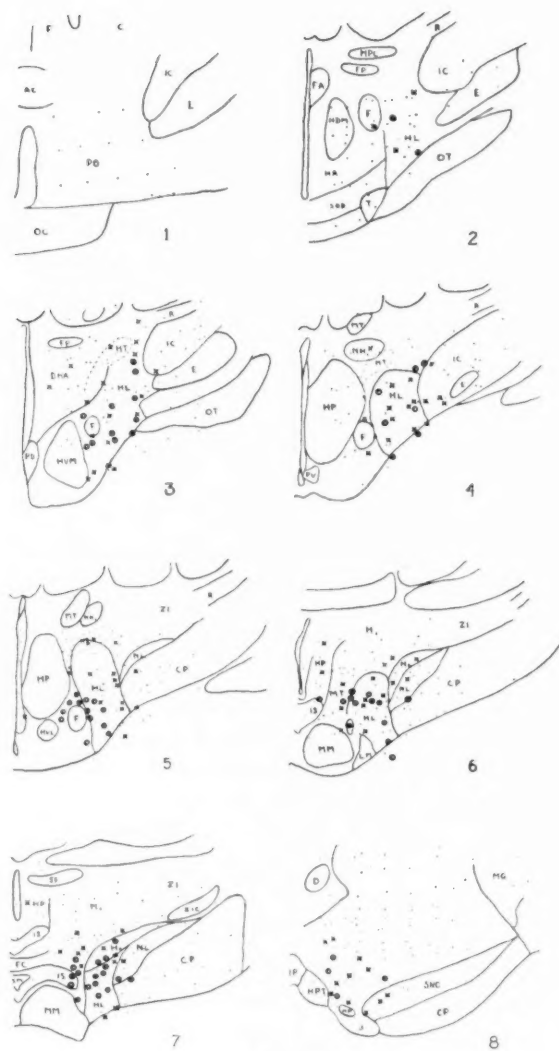


Figure 1

## EXPLANATION OF FIGURE 1

Fig. 1.—Location in the hypothalamus of the points yielding respiratory acceleration and running movements. The circles show the location of points yielding marked respiratory acceleration, the crosses represent points yielding slight respiratory acceleration (less than a doubling of the rate), while the dots mark points the stimulation of which produced no change in the rate of respiration. The figures are arranged rostro-caudally, and extended from the preoptic region (1), through the hypothalamus (2-7) to the commencement of the midbrain (8). The abbreviations used in the figures are: *AC*, anterior commissure; *AHA*, anterior hypothalamic area; *C*, caudate nucleus; *CP*, cerebral peduncle; *D*, nucleus of Darkschewitch; *DHA*, dorsal hypothalamic area; *E*, entopeduncular nucleus; *F*, fornix and perifornical nucleus; *FA*, anterior filiform nucleus; *FC*, supramammillary portion of the commissure of Forel; *FP*, principal filiform nucleus; *H<sub>1</sub>*, field *H<sub>1</sub>* of Forel; *H<sub>2</sub>*, field *H<sub>2</sub>* of Forel; *HA*, anterior hypothalamic nucleus; *HDM*, dorsomedial hypothalamic nucleus; *HL*, lateral hypothalamic area; *HP*, posterior hypothalamic nucleus; *HPC*, parvocellular hypothalamic nucleus; *HPT*, habenulo-peduncular tract; *HT*, hypothalamico-tegmental tract; *HVL*, ventrolateral hypothalamic nucleus; *HVM*, ventromedial hypothalamic nucleus; *IC*, internal capsule; *IP*, interpeduncular nucleus; *IS*, interstitial nucleus of supramammillary decussation; *LH*, lateral habenular nucleus; *LI*, nucleus limitans; *LM*, lateral mammillary nucleus; *LP*, posterior part of the lateral nucleus; *MG*, medial geniculate body; *MH*, medial habenular nucleus, *MM*, medial mammillary nucleus; *MP*, mammillary peduncle; *MT*, mamillothalamic tract; *NH<sub>1</sub>*, nucleus of field *H<sub>1</sub>* of Forel; *NL*, nucleus of Luys; *O*, ovoid nucleus; *OC*, optic chiasm; *OT*, optic tract; *P*, posterior nucleus; *PC*, posterior commissure; *PD*, dorsal periventricular nucleus of the hypothalamus; *PO*, preoptic region; *PP*, posterior part of the pulvinar; *PRE*, pretectal area; *PU*, pulvinar; *PV*, ventral periventricular nucleus of the hypothalamus; *R*, reticular nucleus; *SF*, subparafascicular nucleus; *SFC*, subfornical component of the medial forebrain bundle; *SG*, suprageniculate nucleus; *SNC*, central substantia nigra; *SOD*, diffuse supra-optic nucleus; *T*, tangential nucleus; *ZI*, zona incerta; *ZIC*, caudal zona incerta; 3, oculomotor nerve. Each figure presents the data obtained from all of the cats in which that level was stimulated. The level represented by 1 was stimulated in three cats, by 2, in three cats, by 3 in six cats, by 4 in four cats, by 5 in five cats, by 6 in seven cats; by 7 in eight cats, and by 8 in seven cats; 9 to 16 represent this same series of eight levels, and the respective number of cats is the same as that just given; 17 presents the data from two cats, 18 from one cat, 19 from two cats, 20 from eight cats and 21 from seven cats.

taken into consideration. There was never any rise in temperature; on the contrary, a fall often took place, but a correlation of this with stimulation could not be made.

A marked acceleration in the respiratory rate was characteristically obtained from stimulation in the lateral hypothalamic area and in the region around the fornix. The number of inspirations per minute under experimental conditions, but before stimulation, varied between 20 and 30. Appropriately located stimuli would immediately increase this rate to 90 or 100 inspirations per minute. Cessation of stimulation was not followed by a period of apnea but by a rather rapid return to a normal rate. Sometimes after repeated punctures the rate became permanently increased. In one case, in which respiration of over 90 a minute continued until the animal was killed, extensive hemorrhage was found in the hypothalamus. Under such circumstances, renewed stimulation caused a further temporary increase. The highest rate so obtained was 140 inspirations per minute. In determining the effect of any given stimulus, the rate per minute during stimulation was compared with the rate when the respiration had become stabilized after the cessation of the stimulation. Associated with the rapid respiration, running movements often began as the stimulus was continued, and sometimes also a turning of the head from side to side. Such movements occasionally became so violent as to necessitate holding the animal in the hammock in which it lay or discontinuing the stimulus.

These reactions of widespread excitation within the nervous system were obtained from stimulation in the lateral hypothalamic area and in the region around the fornix (fig. 1). The preoptic area and the level of the anterior hypothalamic nucleus were silent (fig. 1, 1). The first responses were seen about 0.5 mm. behind the optic chiasm at a level just rostral to the rostral pole of the ventromedial hypothalamic nucleus (fig. 1, 2). At the level of this nucleus they became numerous (fig. 1, 3). More caudal levels through the posterior hypothalamic nucleus (fig. 1, 4 and 5) and the mammillary body (fig. 1, 6 and 7) showed many responses. Behind the mammillary bodies, at the level of the posterior commissure, the responses were obtained from about the same dorso-ventral area, but were here much closer to the midline (fig. 1, 8). In the figures great acceleration of respiration is indicated by circles. Points yielding a moderate increase but less than a doubling of the rate are marked with crosses. These are somewhat more widely distributed than the circles, but in general are confined to the lateral hypothalamic area. Naturally, the intensity of the response decreased as the depth of the supplemental ether anesthesia increased, and some of these mild responses may be explained in this way. It will be seen, however, that at some of the levels they are arranged in a zone lying dorsal or dorso-lateral to the field occupied by the circles.

At the beginning of each experiment a thread was passed through the nictitating membrane, which was drawn medialward, and another through the upper lid, which was drawn upward. This kept the pupil fully exposed, but prevented observations on the nictitating membrane.

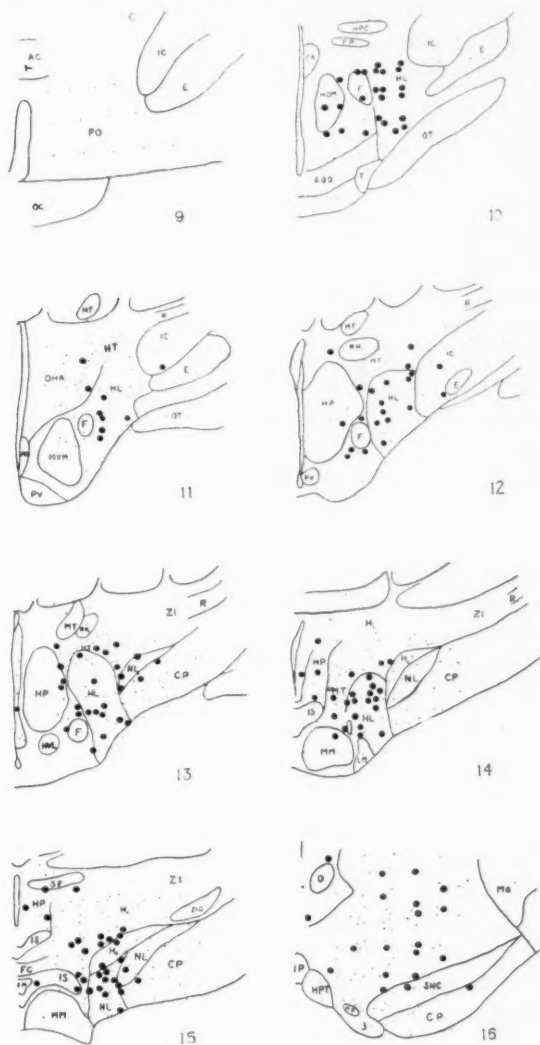


Fig. 2.—Locations from which was obtained marked dilatation of the pupils, indicated by the solid circles, while the dots indicate points the stimulation of which did not produce this response. This figure represents respectively the same series of levels as did figure 1.

The points which on stimulation yielded marked dilatation of both pupils were not as localized in the hypothalamus as were those from

which acceleration of respiration could be obtained. In general, however, the lateral hypothalamic area and the region surrounding the fornix appeared to be the locus from which dilatation was obtained (fig. 2). The preoptic area was silent (fig. 2, 9). Neither the periventricular system nor the subthalamic nucleus appeared to be especially concerned with the response. Occasionally, marked dilatation was obtained from points close to the ventricular wall (fig. 2, 13 to 15) and in the subthalamic nucleus of Luys, especially in its medial part where it lies against the lateral hypothalamic area. At the level of the rostral end of the mammillary body, where the nucleus of Luys is separated from the lateral hypothalamic area by the  $H_2$  field of Forel, its stimulation did not cause marked dilatation of the pupil (fig. 2, 14). Slight dilatation of the pupil could be obtained from almost any point in the hypothalamus; these slight responses have not been plotted in the diagrams. Marked dilatation sometimes resulted from stimulations as far dorsad as the subparafascicular nucleus (fig. 2, 15). At the rostral end of the mesencephalon the reaction became diffuse within that part of the tegmentum which lies ventral to a line drawn through the cerebral aqueduct.

In considering the location of the points yielding respiratory acceleration, running movements and marked dilatation of the pupils, it is important to note that these responses are not obtained from the preoptic region, nor from the median forebrain bundle or fornix in the rostral portion of the hypothalamus. This eliminates the possibility that they are elicited from stimulation of an olfactory pathway. Similarly, the main body of responses appear definitely lateral to the medial hypothalamic nuclei. Nor are these medial nuclei known to send any prominent descending pathway into the lateral hypothalamic area, to which we might allocate the reactions.

The responses are obtained from the lateral hypothalamic area and a region surrounding the fornix. An examination of the work of Malone<sup>5</sup> (1914) and Morgan<sup>6</sup> (1930) shows a striking similarity between the distribution of the nucleus tuberomammillaris, which Malone differentiated on the basis of cell type, and the distribution of the excitable points as shown in our figures 1 and 2. The more caudal responses which have been followed into the rostral part of the midbrain (figs. 1, 8 and 2, 16) evidently represent stimulation of the descending pathway for these reactions.

In the rostral portion of the hypothalamus, a series of typical "spitting" movements, such as a cat makes when confronted with a dog

5. Malone, E. F.: *The Nuclei Tuberis Lateralis and the So-Called Ganglion Opticum Basale*, Johns Hopkins Hosp. Reports, 1914, Monograph no. 6.

6. Morgan, L. O.: *Cell Groups in the Tuber Cinereum of the Dog, with a Discussion of Their Function*, J. Comp. Neurol. **51**:271, 1930.

(opening of the mouth, baring of the teeth with forced expiration), were obtained from stimulation in the locality of a small longitudinal bundle of fibers outlined by dotted lines in figure 3. This bundle appeared to arise from the medial preoptic and medial parolfactory areas and to run through the anterior hypothalamic area (fig 3, 17) to turn laterad into the medial forebrain bundle at the level of the rostral pole of the ventromedial nucleus (fig. 3, 18). The fact that the spitting was not obtained caudad to the ventromedial nucleus, however, might indicate that some of the fibers terminate in that nucleus. This bundle has not previously been described in the cat, but appears to be homologous with the subformical component of the medial forebrain bundle of the rat as described by Krieg<sup>7</sup> (1932).

Bilateral constriction of the pupils was elicited from stimulation of the optic tract as it swings dorsolaterally out of the chiasm (fig. 4, 19). The lateral course of the tract soon removes it from the explored field and the bilateral constriction only reappeared at the caudal limit of the

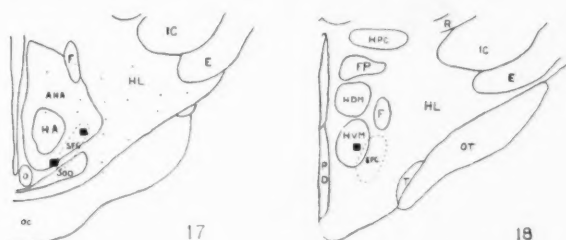


Fig. 3.—Location of points, indicated by solid black squares, which yielded "spitting" movements on stimulation. The dots indicate the points which did not give this reaction. Both 17 and 18 are seen to be from the rostral portion of the hypothalamus.

diencephalon at the level of the posterior commissure (fig. 4, 21). Points yielding this response were found in the pretectal area. Similar points were found along the line of separation between the central gray matter and the tegmentum and may indicate the presence in this region of fibers arising from optic centers of the diencephalon and curving ventrad to reach the Edinger-Westphal nuclei after partial decussation. But since the rostral margin of the superior colliculus is only about 1.5 mm. caudal to this level the question arises as to the possibility of an escape of current to the tectobulbar fibers. In this connection we have reexamined the original records of the mesencephalic stimulations carried out by Ingram, Ranson, Hannett, Zeiss and Terwilliger<sup>3</sup> (1932), and found that they also obtained bilateral pupillary constriction from stimulation of the pretectal area, the nucleus of the posterior com-

7. Krieg, W. J. S.: The Hypothalamus of the Albino Rat, *J. Comp. Neurol.* 55:19, 1932.

missure and the central tegmental fasciculus at the level of the posterior commissure. They obtained the same reaction from stimulation of the optic tract. But from stimulation of the optic stratum of the superior colliculus and the fibers of the tectospinal tract as they encircle the central gray they obtained dilatation of the pupils. It is of interest that in their extensive explorations of the hypothalamus, subthalamus and mesencephalic tegmentum they obtained pupillary constriction only from the optic tract and from the pretectal area and the region of the posterior commissure. Thus their results fully coincide with ours. Sachs<sup>8</sup> (1909), in his experiments on monkeys, found that "a very sharp, quick contraction of the pupils was obtained from a spot where the outer part of the posterior commissure crosses behind Meynert's bundle," which is in essential agreement with our findings. Papez and Freeman<sup>9</sup>

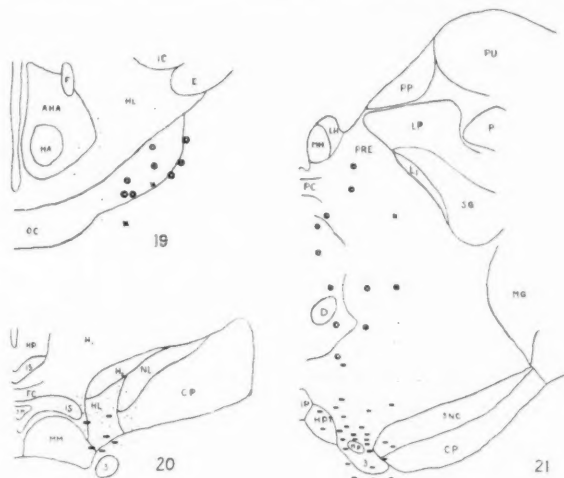


Fig. 4.—Location of points which gave constriction of the pupil. A circle indicates bilateral constriction of the pupils, a cross indicates a slight bilateral constriction, a bar refers to constriction of the pupil of the same side only, while dots represent points which gave none of these responses on stimulation. The level of the optic chiasm is shown in 19, that of the caudal hypothalamus in 20 and that of the posterior commissure in 21.

(1930), after producing lesions lateral to the posterior commissure in the rat, traced degenerating fibers across the commissure and down to the ciliary nucleus of the opposite side. After extensive lesions in the superior colliculi they did not describe any degenerating fibers running through the posterior commissure. The evidence seems to indicate that

8. Sachs, E.: On the Structure and Functional Relations of the Optic Thalamus, *Brain* **32**:95, 1909.

9. Papez, J. W., and Freeman, G. L.: Superior Colliculi and Their Fiber Connections in the Rat, *J. Comp. Neurol.* **51**:409, 1930.

the arc for the pupillary light reflex passes through some nucleus in the posterior part of the thalamus, perhaps the pretectal area or the nucleus of the optic tract, rather than through the superior colliculus or that the tectobulbar fibers for the Edinger-Westphal nucleus arch rostrad into the level of the posterior commissure. But before any such conclusions are reached, the question must be carefully restudied in an investigation specifically directed to that end.

Ipsilateral constriction, with associated ocular movements, was obtained from stimulation close to the oculomotor nerve as it passes forward under the caudal part of the hypothalamus (fig. 4, 20). At the level of exit of the third nerve ipsilateral constriction was a very common response (fig. 5, 21). Often at these levels a stimulus produced concurrently an ipsilateral constriction and a contralateral dilatation of the pupil. This is interpreted as the result of stimulation of a general dilator field through which fibers from the Edinger-Westphal nucleus run, the effect from these constrictor fibers dominating in the ipsilateral side.

#### COMMENT

The extensive literature bearing on the temperature-regulating capacity, the control of metabolism and the relation of the hypothalamus to diabetes insipidus need not be reviewed, since our exploratory results do not throw any light on these functions.

Pupillary dilatation and acceleration of respiration are produced by stimulation of afferent nerves and by stimulating central afferent paths such as the spinothalamic tract (Sachs,<sup>4</sup> 1911; Ingram, Ranson, Hannett, Zeiss and Terwilliger,<sup>3</sup> 1932). For this reason it is important to note that the parts of the hypothalamus yielding these reactions do not contain such tracts, excepting perhaps secondary or tertiary olfactory fibers in the medial forebrain bundle. But these are excluded as factors, since the response is not obtained from this bundle in the preoptic region. It seems likely, however, that the hypothalamus is excited more or less indirectly through the thalamus or the tegmentum of the brain stem when sensory nerves or the pain paths are stimulated, and that in this way the so-called emotional responses to these stimuli are evoked.

The important part played by the hypothalamus in emotional excitement has been made clear by the investigation of Bard<sup>10</sup> (1928, 1929), whose hypothalamic cats exhibited sham rage. In these animals, from which the cerebral hemispheres, corpora striata and cranial half of the diencephalon had been removed, struggling and snarling were accompanied by erection of hair, a rise in blood pressure and secretion of

10. Bard, P.: A Diencephalic Mechanism for the Expression of Rage with Special Reference to the Sympathetic Nervous System, *Am. J. Physiol.* **22**:490, 1928; The Central Representation of the Sympathetic System as Indicated by Certain Physiologic Observations, *Arch. Neurol. & Psychiat.* **22**:230 (Aug.) 1929.

sweat, indicating an activation of the sympathetic system. The typical picture of sham rage included a rapid, panting respiration. But acceleration of respiration does not appear to have been a constant feature of the reaction; in one case during an exhibition of rage the respiratory rate was 240; in a second case, a normal rate of from 20 to 30 during much of the rage, while in a third case, in which no rage was exhibited, there was a rate of 150.

Somatic movements were characteristically present during the rage exhibited by Bard's cats, but as the animals were tied down it is difficult to tell just what these movements may have represented. The work of Hinsey, Ranson and McNattin<sup>11</sup> (1930) is important in this connection. Their hypothalamic cats often showed periods of restlessness in which they would walk about the room. These periods were always preceded and accompanied by a rapid forced respiration. Such behavior is strikingly analogous to the reactions observed in this series of experiments from stimulation of the lateral hypothalamic area.

Stimulation of the wall of the third ventricle in a hemidecerebrate cat was shown by Beattie, Brow and Long<sup>12</sup> (1930) to produce no change in respiration. Cardiac arrhythmia was elicited by such stimulation and, after midline lesions of the periventricular formation, degenerated fibers were seen to pass back into the midbrain, in relation to the aqueduct, to descend to the intermediolateral cell column of the thoracic and upper lumbar cord. Such a lesion was regarded by these workers as serving the posterior hypothalamus from lower centers. Our results show that the periventricular substance is not specifically related to the respiratory and pupillary responses. Because of this fact and because both of these reactions may be traced from the hypothalamus into the midbrain by way of the lateral hypothalamic area, it should be emphasized that the fibers degenerating into the midbrain, in relation to the aqueduct, from Beattie, Brow and Long's midline lesions do not represent the only efferent pathway from the hypothalamus.

The center for pupillary dilatation was located in the neighborhood of the rostromedial part of the subthalamic nucleus by Karplus and Kreidl<sup>1</sup> (1910). Since that time this and other sympathetic functions, such as secretion of sweat and vasomotor reactions, have been assigned to that nucleus (Greving,<sup>13</sup> 1931). But it is important to note that

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11. Hinsey, J. C.; Ranson, S. W., and McNattin, R. F.: The Rôle of the Hypothalamus and Mesencephalon in Locomotion, *Arch. Neurol. & Psychiat.* **23**:1 (Jan.) 1930.

12. Beattie, J.; Brow, G. R., and Long, C. N. H.: The Hypothalamus and the Sympathetic Nervous System, *A. Research Nerv. & Ment. Dis. Proc.* **9**:249, 1930.

13. Greving, R.: Die vegetativen Zentren im Zwischenhirn, in Müller: *Lebensnerven und Lebenstrieb*, Berlin, Julius Springer, 1931.

Karplus<sup>14</sup> (1930) has recently refused to accept responsibility for any such exact localization. He said:

"Wir wollen aber nicht behaupten, dass das Corpus subthalamicum dieses Zentrum sei oder dass etwa die Linsenkernschlinge bei der Reflexübertragung unentbehrlich sei. Die Gegend des Hypothalamus, in der diese Gebilde gelegen sind, gehört offenbar zu dem zentralen Mechanismus; allein zu einer sicheren genauen Feststellung aller hier in Betracht kommenden anatomischen Grundlagen wird es noch so mancher Arbeit bedürfen." Trotz dieser, wie mir scheint, klaren Sprache und obwohl wir in sechs weiteren Mitteilungen auf die anatomischen Verhältnisse dieser Gegend uns nicht mehr bezogen haben, taucht im Schrifttum immer wieder die irrthümliche Auffassung auf, wir hätten behauptet oder gar bewiesen, das Corpus subthalamicum sei das Zentrum für eine Reihe von vegetativen Funktionen. Tatsächlich ist über das Verhältnis der einzelnen anatomischen Kerne im Hypothalamus zu der physiologisch festgestellten Bedeutung dieser Gegend wohl noch lange nicht das letzte Wort gesprochen.

("However, we do not want to assert that the corpus subthalamicum is this center or that perhaps the ansa lenticularis is indispensable in the reflex transmission. The region of the hypothalamus, in which these formations are located, evidently belongs to the central mechanism; however, for an exact determination of all anatomic foundations involved here, much work is necessary." In spite of this, as it appears to me, clear statement, and although in six further reports we made no further reference to the anatomic conditions of this region, in the literature again and again the erroneous opinion springs up, as if we had asserted or even proved, the corpus subthalamicum to be the center for a number of vegetative functions. Actually, the last word has not yet been spoken about the relations of the different anatomic nuclei in the hypothalamus to the physiologically demonstrated significance of this region.)

Sachs<sup>8</sup> (1909) found that stimulation of the pulvinar caused dilatation of the pupil. The same result has been obtained from stimulation of some other parts of the brain (Parsons,<sup>15</sup> 1901; Huet,<sup>16</sup> 1911). References to other work on this subject will be found in the paper by Ingram, Ranson and Hannett,<sup>17</sup> 1931.

An examination of figure 2, 13, 14 and 15 (NL) will show, as do other data not figured, that the pupillary reaction bears no specific relation to the nucleus of Luys. This confirms the conclusions of Ingram, Ranson and Hannett<sup>17</sup> that dilatation of the pupils can be obtained from many other regions in addition to the subthalamie nucleus. In fact, the data expressed in figure 2, 13 to 15 indicate that when this reaction is obtained from the subthalamie nucleus it is to be explained as due

14. Karplus, I. P.: Ueber die Empfindlichkeit des Hypothalamus, Wien. klin. Wchnschr. **43**:623, 1930.

15. Parsons, J. H.: On the Dilatation of the Pupil from Cerebral Stimulation, J. Physiol. **26**:38, 1901.

16. Huet, W. G.: Zwischenhirn und Halssympathicus, Arch. f. d. ges. Physiol. **137**:627, 1911.

17. Ingram, W. R.; Ranson, S. W., and Hannett, F. I.: Pupillary Dilatation Produced by Direct Stimulation of the Tegmentum of the Brain Stem, Am. J. Physiol. **98**:687, 1931.

to a spread of current to the lateral hypothalamic area. The fact that dilatation of the pupils has been erroneously assigned to the nucleus of Luys throws open to question the location there of other sympathetic functions, and indicates that further investigation of such localization is needed.

Karplus and Kreidl<sup>1</sup> have shown that pupillary dilatation can be elicited by stimulation of a point near the frontal pole of the brain. This response could be eliminated by a lesion made with an electrocautery in the corresponding side of the hypothalamus. Nevertheless, the fact that weeks after the removal of the frontal cortex pupillary dilatation could still be obtained by stimulation of the hypothalamus shows that it is more than a mere passageway for dilator fibers from the cortex.

In agreement with Ingram, Ranson and Hannett,<sup>17</sup> our results show that pupillary dilatation of varying degrees can be obtained from almost any part of the hypothalamus, but we have plotted in the diagrams only the marked responses. The authors just mentioned carried their explorations farther back, and found that they could obtain this reaction from practically anywhere in the reticular formation of the tegmentum throughout the mesencephalon and pons. The results of Ingram, Ranson and Hannett, together with the data reported here, enable us to form a connected picture of the path of the dilator fibers in the upper part of the brain stem. Responses of bilateral dilatation of the pupils appear in the rostral part of the lateral hypothalamic area. They descend in that area through the hypothalamus. At the transition to the midbrain they become diffused through the reticular formation of the tegmentum. Scattered throughout the reticular formation of the tegmentum they descend through the mesencephalon and pons. The fact that numerous effective points are found in the midline just caudal to the mammillary body indicates that some crossing occurs at this level, but as the responses are still bilateral in the pons, a further decussation below the pons must take place.

#### SUMMARY

The hypothalamus of each of twenty-two cats was explored with electrical stimulation, the Horsley-Clarke instrument and a bipolar needle electrode being used.

Marked respiratory acceleration associated with running movements was obtained from stimuli in the lateral hypothalamic area and in the region surrounding the fornix. The responses appeared at the level of the rostral pole of the ventromedial hypothalamic nucleus, were numerous throughout the course of the lateral hypothalamic area caudal to this level, and at the transition to the midbrain were obtained from the ventromedial angle of the tegmentum close to the exit of the third nerve.

Marked bilateral dilatation of the pupils was not as limited a response as the respiratory acceleration but, in the main, was obtained from the lateral hypothalamic area and the region surrounding the fornix. The pupillary reactions appeared at the level of the anterior hypothalamic nucleus, extended for the course of the lateral hypothalamic area caudal to this level, and at the transition to the midbrain became scattered through the reticular formation of the tegmentum.

Bilateral constriction of the pupil resulted from stimulation of the optic tract, the pretectal area and points near the line of separation between the central gray matter and the tegmentum at the level of the posterior commissure.

Spitting movements were obtained from stimulation at the level of the supra-optic commissures in the region of the subfornical component of the medial forebrain bundle.

The interpretation of these results in the light of knowledge of the anatomy of the hypothalamus is discussed.

#### DISCUSSION

DR. ROY GRINKER: At the University of Chicago, Leiter and I have been working on the hypothalamus with a different objective. We were interested in determining whether vasomotor centers actually exist in that region as originally postulated by Karplus and Kreidel. At this time I may state that the evidence for such centers is not adequate in the original work or in the confirming experiments of Brow, Beatty and Long. In a paper to be published soon we will report our negative results.

However, we were aware of the work of Aschner, who, in 1912, found that dyspnea resulted from stimulation of the hypothalamus. In our tracings we have graphic evidence that an increase in the rate and amplitude of respiration occurs from hypothalamic stimulation. The sites from which such reactions could be elicited were almost anywhere in the hypothalamus. We, too, found that pupillary dilatation could be evoked by stimulation anywhere in the hypothalamus. Unsheathing of the claws was observed only once and erection of the hairs never. Thus, our incidental observations tend to confirm Dr. Ranson's findings, which indicate a relatively wide hypothalamic area from which pupillary and respiratory changes can be evoked.

I wish to ask Dr. Ranson whether, in view of the fact that such a wide area of the hypothalamus, when stimulated, will modify two seemingly rather important functions, namely, pupillary and respiratory reactions unrelated with specific nuclear areas, he thinks that so-called hypothalamic centers exist, or whether this structure does not act as a whole for many varieties of vegetative functions, and whether the type of reaction differs perhaps with the source of the stimulus.

DR. PERCIVAL BAILEY: It seems rather unusual that Dr. Ranson did not obtain other effects, such as erection of the hair and protrusion of the nails, which are obtained so easily by the removal of the hemispheres, and which are interpreted as release phenomena.

DR. S. W. RANSON: Dr. Grinker's observations in relation to blood pressure are particularly interesting. We were not able to make blood pressure tracings of our animals because of the difficulty of making blood pressure tracings under the conditions of our experiment.

As to whether the hypothalamus functions as a whole or whether there are special centers, I should not care to hazard a guess. There are fairly well defined nuclear masses in the hypothalamus, and a tremendous amount of work will have to be done before we can arrive at any conclusion, but so far as our results on respiration and the pupil are concerned, it is clear that the whole lateral hypothalamic area is involved, but not the median to any considerable extent. In this respect there does not seem to be a differentiation between the median and the lateral portions of the hypothalamus.

Why we did not obtain a reaction of the hair along with the dilatation of the pupil is a mystery to us also. We watched carefully, but did not get it. As I mentioned, we obtained other evidences of excitation. When the stimulus was continued for any length of time the animal would begin to show running movements and would swing his head from side to side and exhibit definite evidences of general excitation.

## INVOLVEMENT OF THE FACIAL NERVE IN MALIGNANT HYPERTENSION

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Malignant hypertension may present a clinical picture strongly suggesting a mass lesion of the brain, with headache and choked disk as the outstanding symptoms in each condition. This was emphasized by Pepper<sup>1</sup> in 1931, who also pointed out that occasionally paralysis of a cranial nerve, usually the facial nerve, added to the confusion. Pepper quoted three such cases from the literature, but offered no suggestion as to the method by which the arteriolar changes of malignant hypertension produce the facial paralysis.

Soon after Pepper's publication there appeared in the wards of the University Hospital a patient with typical malignant hypertension recovering from a right peripheral facial palsy and giving a history of a similar palsy one year previously. Uncertainty as to the mode of production of the facial palsy suggested the advisability of reviewing available cases, and of considering various hypotheses. With that thought in mind, the present case is reported, and eight others collected from the literature are reviewed. Four of these are known to be of the peripheral type, and in five the type is uncertain. Four patients had multiple attacks, the greatest number in a single patient being four. The right side was involved in four patients, the left in one, and in four the side was not stated. Another neurologic lesion of some sort was present in four cases.

The following hypotheses are considered: (1) hemorrhage in the pons, involving the motor nucleus or the intrapontile portion of the motor root; (2) involvement of the nerve between its origin from the pons and the internal auditory meatus by increased intracranial pressure or by local pressure by an artery; (3) hemorrhage within the facial canal. For the last hypothesis only is there pathologic support by necropsy.

### REPORT OF CASES

CASE 1.—*History*.—On March 1, 1932, a white girl, aged 18, was admitted to the University Hospital to the neurosurgical service of Dr. C. H. Frazier, as it was

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1. Pepper, O. H. P.: *Pennsylvania M. J.* **35**:75, 1931.

thought that she had a tumor of the brain; she was transferred to the ward of the medical clinic of the hospital of the University of Pennsylvania on March 10. She had been perfectly well until May, 1931, when a peripheral right facial palsy suddenly developed. She received medicine of various kinds, and the condition gradually cleared up. By November, 1931, she considered herself entirely well. In January, 1932, she began to have headaches in the right frontal region, always associated with nausea and vomiting. These attacks occurred about every other week. On February 26, she had a sharp stabbing pain over the mastoid process behind the right ear; this lasted all night. It was less severe on February 27, but became worse again that night. On the morning of February 28, she felt that her face was drawn to the right and, on looking in the mirror, saw that she could not move the right side of the face, close the right eye or wrinkle the right side of the forehead. On February 29, she consulted a physician, who referred her to the University Hospital. She had noted that at times, while reading, vision in the left eye became somewhat blurred. The past medical history revealed only measles in childhood. The family history was without significance. There was no history of exposure to toxic agents.

*Examination.*—On physical examination, the patient was pale but not acutely ill. The right corner of the mouth drooped; the right eye could not be closed; the right side of the forehead could not be wrinkled, and the lips could not be drawn back on the right side. In repose, the mouth was somewhat drawn to the left. Hearing was somewhat impaired in both ears, more markedly on the left. The tick of a watch was heard in the right ear at 20 inches (50.8 cm.), and in the left ear at 5 inches (12.7 cm.). A Rinne test showed a normal formula on both sides. In the Weber test the patient lateralized to the right. An audiometer showed 46.6 per cent loss of hearing in the right ear, and 67 per cent loss in the left. It was thought that the deafness in the left ear was probably of the nerve type.

Ophthalmoscopic examination showed 7 diopters of choking in the left eye, and 6 in the right. The visual fields showed enlargement of the blind spots. The thyroid gland was barely palpable. The blood pressure on admission was 270 systolic and 160 diastolic. The heart was thought to be slightly enlarged, and this was confirmed by orthodiagram. An electrocardiogram was normal except for left axis deviation.

Taste for sweet, salt, bitter and sour was normal on the left side of the tongue, but was lost on the right. Taste in the posterior third unfortunately was not specifically tested. Examination otherwise gave essentially negative results. A blood count revealed: 83 per cent hemoglobin, with 4,300,000 red cells, 9,000 white cells and a normal differential count. Urinalysis showed a cloud of albumin, many casts of all kinds, white cells in small numbers and a specific gravity ranging up to 1.020. A phenolsulphonphthalein renal function test showed 45 per cent of normal function in two hours. The urea nitrogen of the blood was recorded as 28 mg. per hundred cubic centimeters on admission, but later fell to 17 mg. A van Slyke urea clearance test showed 54 per cent of normal function. The plasma chloride of the blood was recorded as 6.13 mg. per cubic centimeter, or 104.8 millimols per liter. The Wassermann reaction of the blood was negative. The basal metabolic rate was +3 per cent at one determination and -13 per cent at another. Lumbar puncture showed 280 mm. of water pressure, with a normal fluid. A Bárány test suggested a supratentorial lesion, probably on the right side. Roentgen examination of the head gave normal results, except for undue prominence of the various sutures of the skull. Electrical reactions of the right side of the face showed mild reactions of degeneration.

*Course.*—During the period of hospitalization, the patient improved slightly. The blood pressure on discharge was 240 systolic and 148 diastolic. There was 4.5 diopters of choking in each eye. There was some subjective improvement. She was discharged on April 6, 1932. On June 8, it was learned that she felt a little better, though the symptoms persisted essentially as before. The facial paralysis was still present. On June 29, the patient took a 2 mile walk. At 1:30 a. m., on June 30, she arose to go to the bathroom. On returning to her room, bleeding began from the nose and mouth, and she lost consciousness. She died five hours later. Necrosy was not performed.

CASE 2 (Monier-Vinard and Puech<sup>2</sup>).—A man, aged 21, first came under observation in the hospital on May 14, 1926, complaining of headache, visual disturbances, faulty digestion and general fatigue. He gave no history of scarlet fever or syphilis. A year before admission, on beginning army service, albuminuria had been found. Elimination of methylene blue (methylthionine chloride, U. S. P.) was impaired. He worked as a chauffeur until Jan. 12, 1926, when he presented an amblyopia that was progressive. An oculist in consultation diagnosed an albuminuric retinitis. He returned to the home of his parents in Nancy, where he was hospitalized. In addition to the amblyopia he complained of headache and some edema of the eyelids and ankles. Albuminuria was again found. He left after several weeks' rest, and returned to Paris to resume his occupation. A little later, the troubles recurred, and he was hospitalized in Paris. The headache was described as being continuous, and generalized, but involving especially the frontal and temporal regions, and as being severe in character. There was considerable diminution in vision. Ophthalmoscopic examination showed neuroretinitis of the azotemic type, with much papilledema. Profuse nosebleeds recurred daily. There were continuous buzzing in the ears, painful cramps in the calves and thighs and aching in the lumbar region. The appetite remained fairly good, but there were distress after eating and occasional vomiting. The face was pale. There was some edema of the ankles. The heart was normal except for a gallop rhythm. The blood pressure was 210 systolic and 120 diastolic. The pulse was regular. The kidneys were not palpable. A few râles were heard over the bases of the lungs. There was marked albuminuria. The urea nitrogen of the blood was 144 mg. per hundred cubic centimeters. The Wassermann reaction of the blood was negative. On May 19, five days after admission, a right facial paralysis was noted; it appeared following an increase in the frontotemporal pains. The paralysis involved equally the superior and inferior parts of the facial distribution. The patient's general condition grew steadily worse, and he died on June 14, 1932. Autopsy was performed.

The kidneys were congested, with adherent capsules; the thickness of the cortex was diminished. The heart was hypertrophied. The lungs were congested. The brain was normal macroscopically. It was sent to Jumentié, working in the laboratory of Dejerine. The pyramid of the petrous portion of the right temporal bone was also removed and sent to the same pathologist. No inflammation was found in the cavity of the middle ear. No lesion was found in the brain stem. However, after decalcification of the section taken from the petrous portion of the temporal bone, sections were made and a hemorrhage was located in the facial canal.

CASE 3 (May<sup>3</sup>).—A man, aged 37, came under observation on Feb. 27, 1924. The illness dated from the World War, when he had been a prisoner in Germany.

2. Monier-Vinard and Puech: *Bull. et mém. Soc. méd. d. hôp. de Paris* **54**: 977, 1930.

3. May, E.: *Bull. et mém. Soc. méd. d. hôp. de Paris* **54**:915, 1930.

After the armistice he was found to have albuminuria, and his blood pressure was 182 systolic and 120 diastolic. He worked as a reporter until the winter of 1923, when a peripheral facial paralysis, without any painful prodromes, suddenly developed. This gradually cleared up during the following months. Soon cardiac symptoms developed, and in September, 1923, he was hospitalized. Improvement was slow. He was hospitalized again in November, and again in February, 1924, the last time entering the service of May. At that time he had albuminuria, a little edema of the ankles, a blood pressure of 205 systolic and 155 diastolic, and a peripheral facial paralysis. The urea nitrogen of the blood had been 32 mg. per hundred cubic centimeters in September, and was 50 mg. in February. He left the hospital in May and was not followed further.

CASE 4 (May<sup>3</sup>).—A man, aged 36, had been well until May, 1921, when he had the first of four attacks of right peripheral facial paralysis. The first attack lasted until July, 1921; the second, from August to November, 1921; the third, from April to August, 1922, and the fourth began in October, 1922, and was still present on admission, on Oct. 31, 1922. All the attacks came on in the same way. They began with pain in the ear, at the attachment of the sternocleidomastoid muscles and along the border of the trapezius muscle. This pain would last several days and then disappear as the paralysis began. During the third attack urinalysis was done and albuminuria found. A renal condition had not been suspected before. On admission, he also complained of paroxysmal attacks of dyspnea. His blood pressure was 245 systolic and 150 diastolic; the heart was enlarged, but there was no edema. There was marked albuminuria. The urea nitrogen of the blood was 89 mg. per hundred cubic centimeters. The Wassermann reaction of the blood was negative. The patient continued to fail, and died in the middle of December. Autopsy was not permitted.

CASE 5 (Redwood<sup>4</sup>).—A girl, aged 11, complained of headache, pain in the eyes and vomiting. The blood pressure was 230 systolic and 170 diastolic, and the pulse rate was 117. The spinal fluid pressure was 40 mm. of mercury. Papilledema was recorded as 2 diopters on the right and 1 on the left; later, as 5 on the right and 3 on the left. Neurologic examination was performed on Oct. 5, 1924. Definite left facial weakness was noted. Both sides of the body showed some adiadokokinesis. The patellar and ankle reflexes were greater on the right than on the left, and there was a bilateral Babinski sign. The patient was mentally sluggish and drowsy. The urea nitrogen of the blood was normal. The patient died in March, 1925, after an operation for decompression had been performed. At autopsy, the brain was somewhat edematous, and the walls of the vessels were thickened. No definite cerebral lesions were demonstrated microscopically.

CASE 6 (Amberg<sup>5</sup>).—A boy, aged 9, had had headaches for one year and projectile vomiting for six months. Then facial paralysis had occurred on the right, and had been followed by convulsions. Later, the left eye had turned in, and for a few days vision in both eyes was affected. The spinal fluid was under increased pressure, and there was choking of the optic disks. The systolic blood pressure varied between 230 and 190, and the diastolic, between 180 and 115. The patient died four months after coming under observation.

CASE 7 (Amberg<sup>5</sup>).—A girl, aged 13, had been ill for three years with attacks of headache and vomiting. There were also frequent epistaxis and hematuria. The systolic blood pressure varied between 218 and 186, and the diastolic, between

4. Redwood, F. H.: *Virginia M. Monthly* **53**:103, 1926.

5. Amberg, S.: Hypertension in the Young, *Am. J. Dis. Child.* **37**:335 (Feb.) 1929.

120 and 100. It was recorded that "facial weakness existed for six months, disappeared, and reappeared." The urine contained a trace of albumin, and there was edema of the optic disks. Lumbar puncture revealed a pressure of 225 mm. of water. It was stated also that "paresis of the left orbicular muscle and unilateral impairment of hearing made the neurologist suspect a lesion of a small cortical vessel in the pons." At the time of the report the patient was living, but was very ill.

CASE 8 (Keith, Wagener and Kernohan,<sup>6</sup> and, also Amberg<sup>5</sup>).—A girl, aged 15, had had headaches for four years and albuminuria for two years. Morning nausea had been present for six months. Facial paralysis had appeared two months before the child came under observation, but had disappeared by the time of admission to the clinic. It had been ascribed to a fall received while running hurdles, though the patient had not struck her head. The blood pressure was 200 systolic and 140 diastolic. There were papilledema and neuroretinitis. Death occurred one year after the patient was first seen.

CASE 9 (Keith, Wagener and Kernohan<sup>6</sup>).—A woman, aged 37, complained of headache, dyspnea, precordial pain and loss of weight for one year before coming under observation. Two weeks before admission she had an apoplectic stroke, and there had been some visual disturbances since. The blood pressure was 240 systolic and 155 diastolic. She had other characteristics of malignant hypertension. She was under observation for about seven months before death, during which it is stated that she had a facial paralysis.

#### COMMENT

In my own case, and in at least three of the others, the paralysis was of the peripheral type. In the other five cases the type is not definitely stated. Consideration of the peripheral type alone would automatically eliminate all lesions occurring above the nucleus of the facial nerve. A brief recapitulation of the anatomy involved would seem to be in order.

The facial nucleus (motor) measures 5 mm. in length and is situated in the posterior portion of the tegmentum of the pons. The fibers arise from the dorsal aspect of the nucleus and pass dorsad and mediad through the *formatio reticularis*. They then bend forward to pass around the nucleus of the sixth nerve and turn sharply upward over the dorsal surface of the nucleus. They then pass ventrad, laterad and somewhat backward to emerge on the lateral aspect of the lower border of the pons, close to the sensory root. The motor and sensory roots, as yet ununited, pass outward to the internal auditory meatus, through which they pass above and anterior to the auditory nerve. At the bottom of the meatus they leave the auditory nerve to enter the facial canal in the petrous portion of the temporal bone. The geniculate ganglion is situated at the genu of the canal, and there the two roots unite to form a single trunk, emerging beyond at the stylomastoid foramen.

6. Keith, N. M.; Wagener, H. P., and Kernohan, J. W.: The Syndrome of Malignant Hypertension, *Arch. Int. Med.* **41**:141 (Feb.) 1928.

men. It is to be noted that the chorda tympani nerve leaves the facial nerve a short distance above the stylomastoid foramen, and, among other functions, supplies taste sensation to the anterior two thirds of the tongue. Its sensory fibers are processes of cells lying within the geniculate ganglion. From the geniculate ganglion afferent fibers pass in the sensory root to the pons, close to the superficial origin of the motor root. On entering the pons, they pass either through or dorsad to the spinal root of the trigeminal nerve to reach the superior part of the nucleus of reception, which they share with fibers of the glossopharyngeal and vagus nerves. From this nucleus axons pass to the mesial fillet of the opposite side, and eventually to the cerebral cortex.

It will thus be seen that there are four locations where lesions causing facial paralysis of the peripheral type might occur. The first of these is in the pons; most suggestive of this would be involvement of contiguous structures, such as other cranial nuclei and the sensory and pyramidal tracts. The second is the intracranial but extrapontile course of the nerve from the pons to the internal auditory meatus. Here the nerve could most readily be affected by general changes in the cerebrospinal fluid system, such as meningitis or increased pressure. Such lesions would be apt to involve the sixth and eighth nerves as well. The third portion lies within the facial canal. It may become involved in infections of the middle ear. The fourth part is at the point of emergence from the stylomastoid foramen, where the nerve is exposed to external irritants, the most important of which is cold. The tract for taste, supplying the anterior two thirds of the tongue, passes through the chorda tympani to the facial nerve within the facial canal, and then via the single trunk to the geniculate ganglion. From the ganglion it courses in the sensory root as already described. Lesions of the nerve at its origin from the stylomastoid foramen, such as those caused by refrigeration, would therefore not ordinarily involve loss of taste; neither would lesions involving the motor nucleus or the intrapontile part of the motor root. It might be hazarded, therefore, that the most likely location for a lesion causing facial paralysis with loss of taste, not complicated by other neurologic lesions, would be in the facial canal. It has been stated, however, that the paralysis due to refrigeration can extend centrally, and occasionally causes loss of taste as well.

In cases 1, 2, 3, 4 and 8, no neurologic lesions have been definitely established other than the facial paralysis, unless the slight deafness in case 1 is considered. In case 2 a hemorrhagic lesion was definitely located at autopsy in the facial canal. In my case (case 1), one is tempted to hypothecate a similar lesion, partially supported by the loss of taste. It is interesting that in both these cases, as well as in case 4, severe pain preceded by some time, in my case by nearly forty-eight

hours, the onset of the actual paralysis. In case 5 there was definite evidence of disease of the pyramidal tract, which would suggest a lesion in that part of the pons, possibly quite small. The findings at necropsy about five and a half months later, reported as negative, do not rule out this hypothesis. Unless serial sections were made a small area of gliosis could readily be missed. In case 6, in addition to the right facial palsy, there was paralysis of the left sixth nerve, which would suggest, perhaps, an increased intracranial pressure effect, involving the nerve between the pons and the internal auditory meatus. In case 7 the same area is suggested by involvement of the eighth nerve plus some imbalance of the left ocular muscles, though a pontile lesion could well do the same thing.

Certain other facts in the histories of the cases deserve comment. Of the nine cases, five showed a single attack, three two attacks and one four attacks. In four cases the side involved is not known. The left side was involved in case 5, the one in which a lesion in the pons might well be suspected. In the four remaining cases the paralysis was on the right side. I have no explanation for this. One might anticipate that in a larger series of cases the right-sided preponderance would not be maintained.

Pathologic data are inadequate. In the series reported by Keith, Wagener and Kernohan<sup>6</sup> several autopsies were performed; not in the cases showing facial paralysis, however. Small areas of focal softening were found throughout the brain, including the pons. Wilson and Winkelman<sup>7</sup> have stressed the frequency of the occurrence of pontile hemorrhage associated with diverse intracranial conditions. Paralysis of the sixth nerve is recognized as a common complication of any condition causing increased intracranial pressure. Among the theories advanced to account for this are the following: (1) The paralysis is the result of the compression itself; (2) it is the result of traction caused by change in the position of the brain secondary to the compression; (3) it is the result of local pressure from a branch of the basilar artery. The last has been suggested by Cushing (quoted by Foster Kennedy<sup>8</sup>), who has demonstrated gross indentations in nerves crossed by such branches. The same theories might be advanced with less force in the case of the facial nerve. It is to be noted that internal auditory branches from the basilar artery<sup>9</sup> accompany the

7. Wilson, G., and Winkelman, N. W.: Gross Pontile Bleeding in Traumatic and Nontraumatic Cerebral Lesions, *Arch. Neurol. & Psychiat.* **15**:455 (April) 1926.

8. Kennedy, Foster, in *Nelson Loose-Leaf Medicine*, New York, T. Nelson & Sons, 1930, vol. 6, p. 124.

9. Piersol, G. A.: *Human Anatomy*, ed. 7, Philadelphia, J. B. Lippincott Company, 1919, vol. 1, p. 758.

eighth nerve to the internal auditory meatus to supply the internal ear, and so in part of their course must be quite close to the facial nerve as well. A theory making use of arterial pressure is especially appealing in a condition characterized by an enormous increase of that pressure. The possibility of a hemorrhage in the facial canal would seem to be proved by case 2.

#### CONCLUSIONS

Facial paralysis occasionally occurs in malignant hypertension. It is probable that it is caused by one or other of the following: (1) hemorrhage within the facial canal; (2) hemorrhages in the pons; (3) pressure by an artery on the nerve trunk between its point of origin from the pons and the internal auditory meatus; (4) involvement of the nerve in the same area as part of an increased intracranial pressure.

The facial paralysis does not appear to modify in any way the course of the malignant hypertension, but, conversely, malignant hypertension is one of the most serious etiologic factors that can be discovered for a facial paralysis.

## RECOVERY OF SENSATION IN DENERVATED PEDICLE AND FREE SKIN GRAFTS

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AND

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The literature on the recovery of sensation in transplanted skin is extremely scanty. In 1899, Stransky<sup>1</sup> reported a few observations in eleven cases of pedicle flaps and Thiersch grafts in which he described a return of tactile sensibility as early as ten days after transplantation. Dubreuilh and Noel<sup>2</sup> made a few incomplete observations in eleven cases of Wolfe grafts, and found that superficial sensation recovered in about a year. Williams<sup>3</sup> described the presence of impaired sensation in a Thiersch graft thirty years after operation. Davis and Traut<sup>4</sup> made the brief statement that recovery of sensation begins at the periphery of all types of skin grafts in four or five weeks, and that tactile sensibility is restored first, followed by pain and temperature sense. Their method of testing and specific cases are not described. While recovery of sensation is not of major importance in the late results of plastic surgery, skin transplants comprise a valuable type of clinical material for the study of peripheral nerve regeneration and the mechanism of cutaneous sensation.

The literature in the field which deals with recovery of sensation after injury or division of the peripheral nerves has been summarized by Cobb,<sup>5</sup> Lee<sup>6</sup> and Stopford.<sup>7</sup> We shall mention briefly only a few of the reports that are of significance for the findings to be described in

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Read at a meeting of the Chicago Neurological Society, March 17, 1932.

1. Stransky, E.: *Wien. klin. Wchnschr.* **12**:815 and 833, 1899.

2. Dubreuilh, W., and Noel, P.: *Rev. de chir., Paris* **43**:83, 1911.

3. Williams, G. A.: *End-Results in Thiersch Graft: A Case Observed After Thirty Years*, *Arch. Surg.* **16**:938 (April) 1928.

4. Davis, J. S., and Traut, H. F., in Lewis, Dean: *Practice of Surgery*, Hagerstown, Md., W. F. Prior Company, 1931, vol. 5, chap. 8.

5. Cobb, S.: *Cutaneous Sensibility in Cases of Peripheral Nerve Injury: Epicritic and Protopathic Hypothesis of Head Untenable*, *Arch. Neurol. & Psychiat.* **2**:505 (Nov.) 1919.

6. Lee, F.: *Physiol. Rev.* **9**:575, 1929.

7. Stopford, J. S. B.: *Sensation and the Sensory Pathway*, New York, Longmans, Green & Co., 1930.

various types of skin transplants. The original theory of Head,<sup>8</sup> which postulated separate fiber systems subserving epicritic and protopathic sensation, has been widely criticized. Trotter and Davies,<sup>9</sup> Boring<sup>10</sup> and others have failed to confirm Head's findings of spatial and temporal dissociation between two groups of sensation after injury and regeneration of the peripheral nerves. Stopford, however, continued to support Head's hypothesis and subdivided deep sensibility also into protopathic and epicritic forms. Stookey<sup>11</sup> discarded the terminology of Head as misleading and substituted for each modality the name of the stimulus employed, such as pin prick area and cotton wool area. Pollock<sup>12</sup> has reported that the early return of prick pain to an area after injury of the peripheral nerves is due to the presence of adjacent overlapping nerves, and that in the area of exclusive nerve supply pain does not return before touch. Cobb<sup>4</sup> expressed the belief that the apparent dissociations in lesions of the peripheral nerve arise from comparison of stimuli which are quantitatively unequivalent. Burrow and Carter<sup>13</sup> pointed out the danger of arousing deep rather than cutaneous sense when too coarse stimuli are applied.

In order to rule out the possibility of overlap of nerves, Sharpey-Schafer<sup>14</sup> studied the return of sensation in his fifth finger after injury to the nerve supply at the base. When the nerve on the ulnar side of the finger was crushed, complete recovery of all forms of sensation occurred within four months. Pain returned first, followed by sensibility to warm and cold. Touch returned last. On the other side of the finger, where the nerve was cut without resuture, complete recovery did not take place within three years. Hyperalgesia of a distinctly unpleasant character appeared in three months at the proximal end of the finger and gradually proceeded distally. Normal touch did not return, but stimulation even with a von Frey hair gave rise to an unpleasant tingling sensation, which Sharpey-Schafer attributed to faultily insulated regenerating nerve fibers. Warm and cold could be differentiated if contact was avoided. Two findings in Sharpey-Schafer's experiment are noteworthy. First, in an area assumed to be completely denervated by crushing the nerve, there was a temporal dissociation in the return of

8. Head, H.; Rivers, W. H. R., and Sherren, J.: *Brain* **28**:99, 1905.

9. Trotter, W., and Davies, H. M.: *J. Physiol.* **38**:134, 1909. Trotter, W.: *Lancet* **1**:1252 (June 21) 1924.

10. Boring, E. G.: *Quart. J. Exper. Physiol.* **10**:1, 1916.

11. Stookey, B.: *Surgical and Mechanical Treatment of Peripheral Nerves*, Philadelphia, W. B. Saunders Company, 1922.

12. Pollock, L. J.: Overlap of So-Called Protopathic Sensibility as Seen in Peripheral Nerve Lesions, *Arch. Neurol. & Psychiat.* **2**:667 (Dec.) 1919.

13. Burrow, J. L., and Carter, H. S.: *Brit. M. J.* **2**:535, 1918.

14. Sharpey-Schafer, E. A.: *Quart. J. Exper. Physiol.* **19**:85, 1928; **20**:95, 1930.

pain, touch and temperature discrimination. Second, when the intra-neural pattern was disturbed by cutting, recovery was delayed, hyperesthesia was persistent, and touch and temperature remained incomplete. The conception that neurilemmal sheath cells serve as conduits for regenerating nerve fibers after division of the peripheral nerve is generally accepted in the literature. This evidence was reviewed by Kirk and Lewis.<sup>15</sup> Whether or not regeneration takes place only along the neurilemmal sheaths of cut nerves is a question. There is the possibility that the invading nerve fibers penetrate the tissues independently of the old degenerated fibers.

Boeke and Heringa<sup>16</sup> examined histologically nerve endings in a fragment of skin taken for biopsy in a case of partial recovery of sensation, nine months after section and suture of a superficial branch of the ulnar nerve. These investigators found nerve endings incompletely regenerated, the stimulation of which they believed gives rise to so-called protopathic sensibility. When regeneration is complete, the same nerve endings could modulate the more discriminative (epicritic) responses. This hypothesis may explain the fact that recovery of sensation at a given point following suture of a divided nerve occurs gradually and not, as Head believed, in an all-or-none fashion.

#### CLINICAL MATERIAL

A group of patients presenting full-thickness pedicle flaps, Wolfe, Reverdin and Thiersch grafts, has been followed for the return of sensation in the surgical clinic of Dr. D. B. Phemister. In many cases several types of grafts had been made at approximately the same time so that a direct comparison of sensory recovery could be made.

Particular study was made of pedicle flaps, eight of which were followed for extended periods. The flaps were all doubly pedunculated, transplanted by the method of delayed transfer to insure a blood supply adequate for viability. The flaps were undermined and the sides and ends were cut in succession, so that when the transfer had been completed, all the original vascular and nerve connections had been severed. In these, as well as in free grafts, the question of nerve overlap or of collateral innervation is thus completely eliminated. The old neurilemmal relationships are destroyed and, in most flaps, the polarity of the original nerve sheaths has been changed, in some cases all the way from 90 to 180 degrees.

These transplanted flaps constitute a new and ideal terrain for following sensory return, since one has a completely denervated and a well demarcated area of anesthetic skin into which new nerve fibers must

15. Kirk, E. G., and Lewis, D. D.: *Bull. Johns Hopkins Hosp.* **28**:71, 1917.

16. Boeke, J., and Heringa, G. C.: *Nederl. tijdschr. v. geneesk.* **1**:4, 1925.

find their way. Lee<sup>6</sup> has pointed out the neglect of this useful type of clinical material for the investigation of regeneration of the peripheral nerves. The majority of flaps were of sufficient size so that approximate areas of recovery could be plotted at successive examinations.

#### METHOD OF EXAMINATION

While not the same in all cases, tests for sensation in the flaps were usually begun as soon as healing occurred. Some cases have been examined frequently for as long as eighteen months after transplantation. While too much reliance cannot be placed on sensory examinations in clinical subjects, the presence or absence of pain and light touch can be determined and plotted with a fair degree of accuracy by simple methods. For the sake of brevity we have designated appreciation of pin prick, cotton wool and temperature differences simply as pain, touch and temperature sense.

Pain has been tested by the usual pin prick method. Cobb<sup>3</sup> has reported that the area of prick anesthesia varies somewhat with the amount of force applied and suggests the use of an algesimeter for accurate determinations of pain sensibility. In our cases a light pin prick applied with a force not sufficient to stimulate deep sensibility has served satisfactorily to plot approximate areas of recovery. We have checked a number of our results with an algesimeter delivering 14 Gm. of prick by gravity and have found no significant differences.

Light touch has been investigated by applying a fine wisp of cotton wool sufficiently pliable not to indent the skin. The grafts in all but two cases were hairless or contained a few fine lanugo hairs, so that shaving was not required. Light stroking with a camel's hair brush was used occasionally for preliminary testing.

Temperature discrimination was tested by means of Wassermann tubes containing hot water ranging from 45 to 50 C., and cold water ranging from 20 to 25 C. Two-point discrimination was difficult to evaluate in our subjects. Pressure was not studied extensively, since the possibility of stimulating sensation deep to the graft could usually not be eliminated.

All ordinary precautions were observed to make tests as accurate as possible. The subjects were examined after a period of rest in a warm room. A simple affirmative response was given by the patient with his eyes closed as he perceived the touch of cotton or the sharpness of a pin prick. Since the areas involved were small, fatigue was not an important factor. The majority of determinations were checked by two or more observers, including Dr. Roy Grinker in many instances.

The chief questions we hoped to answer were the following: 1. Does partial or complete recovery of cutaneous sensation occur in all types of skin grafts? 2. In what order do the several modalities recover? Is there a temporal dissociation between the recovery of pain and light touch? 3. Does the recovery pattern in pedicle flaps bear any relation to the sheaths of the degenerated nerves?

#### CLINICAL OBSERVATIONS

CASE 1.—G. V. had a disabling defect of the upper lip after excision of a carcinoma (fig. 1*A*). A long visor flap, with its base in the right temporal region, was gradually elevated, detached and swung down to provide a new upper lip (fig. 1*B*). At this stage the distal half of the flap innervated by the supra-orbital

nerve was found to be completely anesthetic, while the proximal half retained sensation from its nerve supply in the temporal region. The pedicle was later sectioned, the unutilized portion was replaced, and Thiersch grafts were applied to the denuded area over the scalp (fig. 1C). The general course of the sectioned nerve fibers of the flap is from the inferior free margin upward, while new nerve

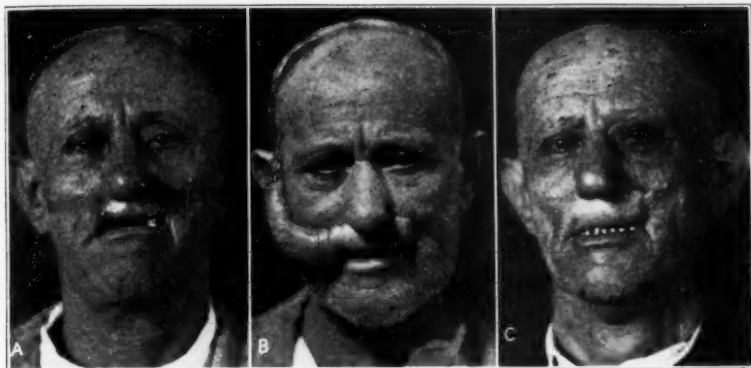


Fig. 1 (case 1).—*A*, defect in upper lip after excision of carcinoma. *B*, pedicle from scalp replacing defect with attachment in temporal region. The distal half is anesthetic. *C*, final result. The temporal portion of the flap has been replaced.

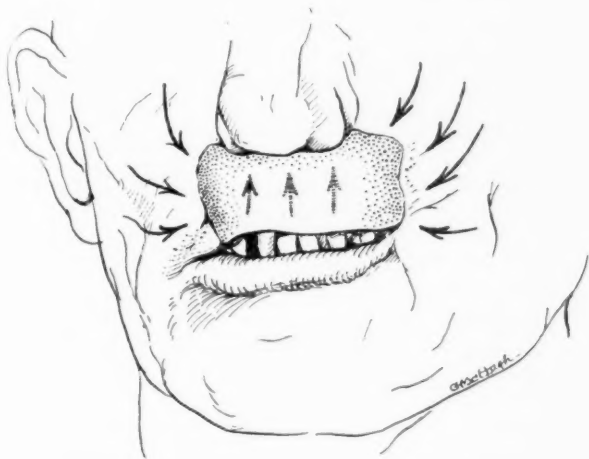


Fig. 2 (case 1).—The stippled area shows recovery of pain at six months. In this and in subsequent diagrams, the broken arrows indicate the course of the original nerve fibers of the flap. The solid arrows indicate the course of surrounding intact cutaneous nerves.

fibers must come in from the lateral and superior margins at angles ranging from 90 to 180 degrees to the course of the degenerated fibers (fig. 2). The gingival surface, which had been Thiersch grafted, retained its epithelial lining and did not become adherent.

Sensory examination after six months revealed the presence of pain in the lateral thirds of the flap and a few spots along the superior margin. At nine months, pain was present throughout the flap, but was of diminished intensity in the central portion, while touch was present but reduced. A few pain spots were present along the anterior margin of the Thiersch graft over the scalp. In ten months, touch seemed present over the entire flap, with delay in recognition. A further return of touch occurred at eleven and at twelve months, although the response remained of decreased intensity in the medial third. In sixteen months, pain and touch were as acute as on the normal skin and were well localized, but temperature discrimination had not returned. At eighteen months, warm at 45 and cold at 20 C. could be distinguished fairly well over the flap. A sweating test was positive only at the upper angles and along the left lateral border of the flap. At this time the Thiersch grafts over the scalp and on the under surface of the lip showed some recovery of pain sense, but no return of touch or of temperature sense.

The recovery of only a few pain spots on the Thiersch grafts is in marked contrast to the almost complete recovery of sensation in the full-thickness flap, in which return of pain had begun in six months, touch in nine, and temperature discrimination in eighteen. Since the lower margin and the inner surface of the flap were free, the course of the invading nerve fibers from the upper and lateral margins was at from 90 to 180 degrees of those of the original nerve fibers of the flap. In addition to the progression of the recovery pattern from the sides, further evidence that the invading fibers course transversely was adduced by the fact that a horizontal biopsy incision at the lateral margin of the flap produced no loss of sensation either above or below.

CASE 2.—T. S. had a visor flap, similar to that in case 1, transplanted to form a new lower lip as a squamous cell carcinoma had been widely excised (fig. 3). Thiersch grafts on the under surface did not take, so that the flap became extensively adherent to the gingival margin.

One month after final section, a few pain spots seemed present at the inferior and lateral borders. These were not sharp, however, and may have represented transmitted pressure. At two and a half months, light pin prick and the pressure of the head of a pin were well perceived and distinguished for 1 cm. along the lateral margins. Both of these had a slight degree of unpleasantness, but did not radiate and were properly localized. Touch and temperature were not present. At three and a half months, pain had advanced to 1.5 cm. along the lateral borders and had assumed a normal quality. A rare response to cotton wool was elicited at the superior angles. Firm pressure at the lateral borders elicited the characteristic tingling of Tinel's sign. Temperature discrimination remained absent. At five months, the prick area had advanced to 2.5 cm. laterally, while touch was fairly good at the superior angles. At six months, touch had become quite accurate at the upper angles for a distance of 1.5 cm. (fig. 4). A rare response to cold was elicited at the lateral borders. At seven months, pain had advanced to cover the entire flap, but was of diminished intensity in the center. Touch continued to progress from the lateral borders, until at ten months it covered half the area of the flap, while some hypalgesia to pin prick persisted in the center. Cold was perceived occasionally along each lateral centimeter, but warmth was not perceived at all. A procaine hydrochloride wheal at the lower left lateral margin produced an anesthesia for 1.5 cm. medially on the flap, while similar wheals at the superior and inferior margins gave rise to no loss of sensation in the flap. This is further evidence that the ingrowing nerve fibers were coming into the flap from the lateral borders.

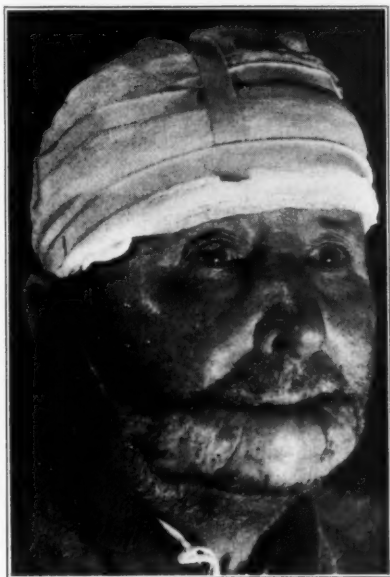


Fig. 3 (case 2).—Pedicule replacing lower lip. The distal half is anesthetic.

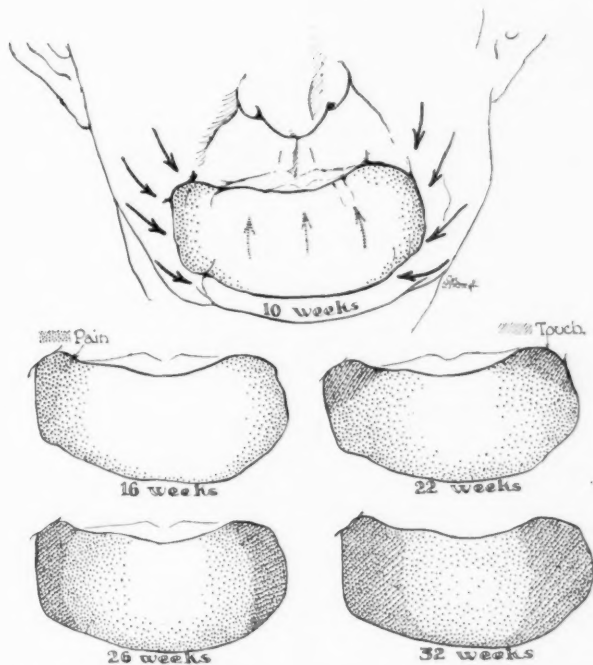


Fig. 4 (case 2).—Areas of recovery of pain and touch at ten, sixteen, twenty-two, twenty-six and thirty-two weeks. Touch was more certain at thirty weeks.

In this flap recovery of pain began in two and a half months and was almost complete in ten months. Touch was present beyond question only at seven months, while some perception of cold appeared at eight months. The recovery pattern for each modality (fig. 4) progresses from the lateral borders at 90 degrees to the course of the old nerve fibers.

Thiersch grafts over the scalp remained completely anesthetic for seven months. A few pain spots, diffusely distributed, appeared at eight months and remained few in number at ten months, at which time about one prick in five was perceived over the anterior and lateral portions. There was no recovery of touch or of temperature discrimination.

CASE 3.—J. C., a boy, aged 9, had a 50 degree flexion contracture of the left knee from scarring subsequent to an extensive third degree burn of the thigh and

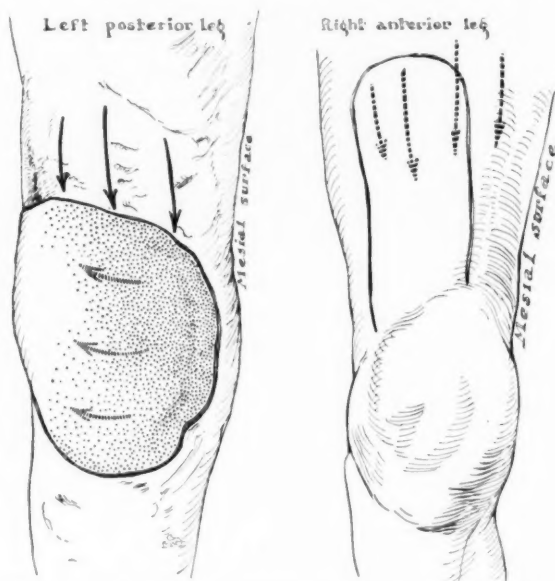


Fig. 5 (case 3).—Flap A placed transversely in left popliteal region. Hypalgnesia along lateral border at eight months.

leg three years previously. The deformity was repaired by full-thickness pedicle grafts from the opposite extremity.

*Posterior Flap A.*—A flap was transferred to the left popliteal space from the anterior surface of the opposite thigh. The polarity of the flap was changed 90 degrees in the course of transplantation. After four and a half months, pain of reduced intensity was present throughout, while touch, if present at all, was very slight. At eight months, pain had become more acute, except along the lateral border (fig. 5), and touch was definitely present. At twelve months, pain and touch seemed as intense as on the opposite popliteal space. Temperature remained absent at thirteen and fourteen months. Warm and cold could be distinguished with some uncertainty from sixteen to nineteen months. The temporal dissociation of sensory recovery was quite definite, with return of pain in four months, touch in eight and temperature sense in sixteen.

*Anterior Flap B.*—A flap over the knee from the opposite calf was transplanted so that the polarity was reversed to 180 degrees. While there seemed to be an early recovery of light pressure, pain was present for the first time at five months, touch at six months and temperature discrimination at nine months. The area of recovery for each modality proceeded in definite progression from the superior and medial portion (fig. 6). Scarring along the lateral border apparently delayed the ingress of new nerve fibers from that portion. At twelve months, pain and touch were complete, while some hypesthesia to warm and cold remained at the inferior-lateral angle.

Thiersch grafts over the right calf after twelve months and those over the right leg three years old showed a poor return of pain and no recovery of touch or of temperature. Reverdin grafts over the calf showed a good response to pin prick but none to cotton wool or to temperature differences. The failure of recovery

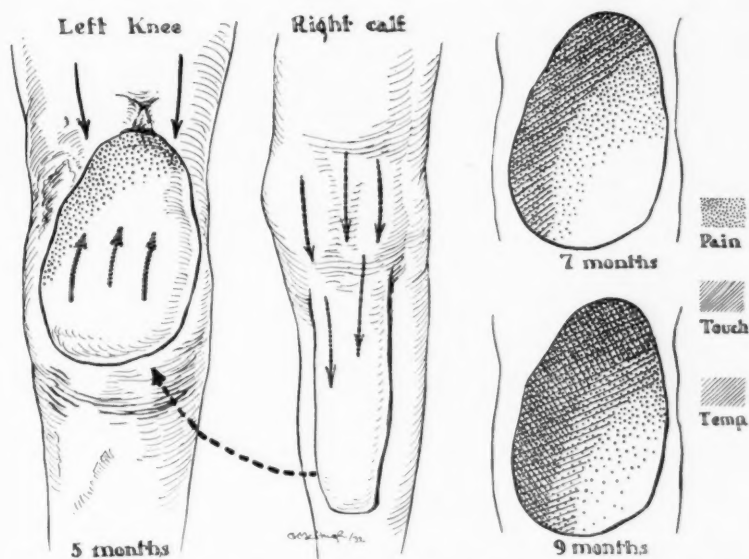


Fig. 6 (case 3).—Flap B over left patella. Polarity reversed. Recovery of pain, touch and temperature from above and medially.

of touch and temperature sense in Thiersch and Reverdin grafts is in marked contrast to the excellent recovery in two pedicle flaps on the same patient.

CASE 4.—W. B., a boy, aged 9, had congenital stricture of the skin of the right leg, syndactylism and maldevelopment of the digits of both hands. A large pedicle flap, 13 by 5 cm., was transferred to the back of the leg with reversal of polarity (fig. 7). At five and six months, pain was present in the upper centimeter, with an occasional response to pin prick in the upper half. At nine months, the pain area included the upper third and at eleven months had advanced to within 1 cm. of the lower border, although the inferior third remained hypalgesic. A small area of touch, 2 by 2 cm., appeared at the superior lateral angle at eleven months and increased to 5 cm. along both medial and lateral margins at seventeen months. There was no recovery of temperature discrimination. A sweating test showed a few small areas of response in the upper portions.

*Wolfe Grafts.*—Three elliptic whole-thickness skin grafts containing no subcutaneous tissue were transplanted from the abdomen directly to the interdigital spaces of the right hand for relief of syndactylism. Pain began to return in these grafts in from five to six months and was apparently normal in twelve months. Slight return of touch was present at eighteen months. Some temperature discrimination seemed present, although response from adjacent normal skin could not be eliminated.

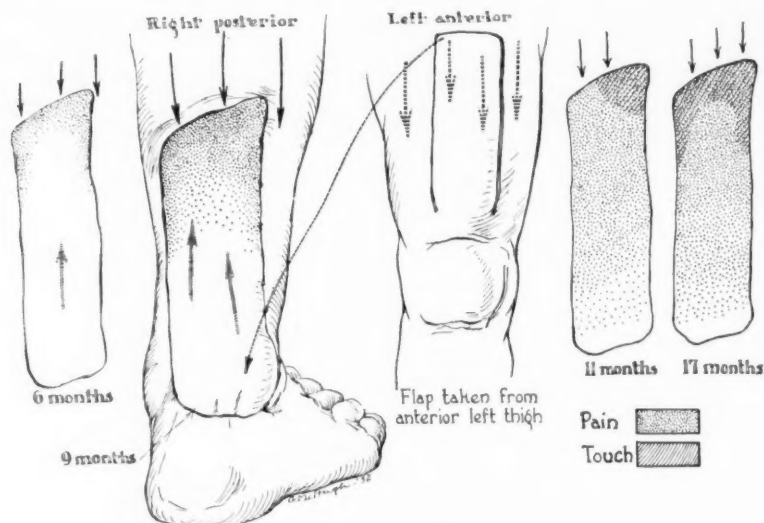


Fig. 7 (case 4).—Large flap from left thigh to right ankle. Polarity reversed. Recovery at six, nine, eleven and seventeen months.

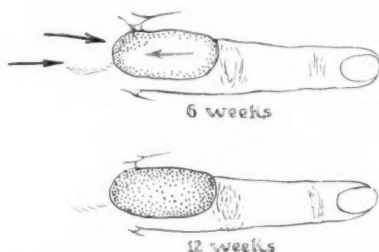


Fig. 8 (case 5).—Pedicle flap from abdomen to finger. Polarity reversed. Definite recovery of pain in three months.

Reverdin grafts over the thigh at eleven and eighteen months showed a good recovery of pain, while Thiersch grafts in the same region gave a diminished response to pin prick. Neither type of graft recovered touch or temperature sense.

CASE 5.—E. L., aged 28, had a pedicle flap from the abdomen to the proximal phalanx of the fourth finger. The polarity of the cutaneous nerves was reversed. A few pain spots appeared at the proximal border and about the periphery in six weeks. In three months, pin prick was well perceived about the periphery

(fig. 8). Touch and temperature sense were not present. Since the patient returned to Sweden, further examinations could not be made.

CASE 6.—H. K., a girl, aged 14, had a scar and an ulcer over the heel replaced by a transverse pedicle flap from the opposite thigh (fig. 9). After seven weeks, some sensation to pin prick was present along the upper centimeter. Within fourteen weeks, the pain area had advanced from above to cover most of the flap, although the response was of normal intensity only in the superior and medial 2 cm. Little further change had occurred in eight months. Touch and temperature had not recovered. Tinel's sign was positive along the upper border.

CASE 7.—S. K., a woman, aged 22, had a large pedicle flap from the thigh sutured transversely over the tibia in an area of extensive cicatrix. No recovery

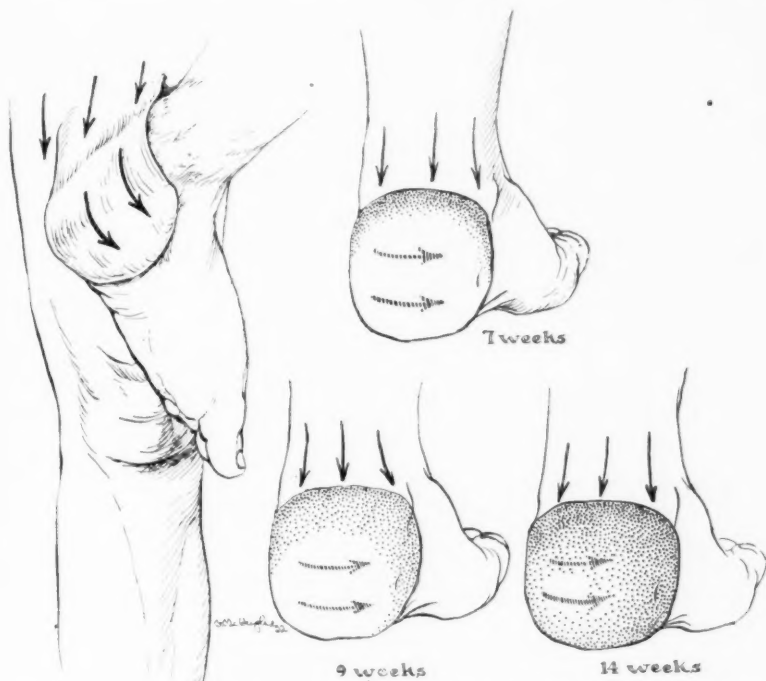


Fig. 9 (case 6).—Flap from thigh to heel. Polarity transverse. Early return of prick pain. Progression from proximal border.

of sensation occurred in fifteen months. The position of this flap directly over bone in an area of dense scar tissue leaves little opportunity for regenerating nerve fibers to find their way into it.

CASE 8.—J. B. had a defect of the heel covered by a transverse flap from the opposite thigh. At three months, pin prick over a small area, noted in figure 10, caused a disagreeable aching sensation, referred anteriorly along the medial side of the foot. The same condition obtained at six months. At ten months, this area of pain recovery had increased to 2 sq. cm., had lost its protopathic quality and was properly localized. Some recovery of pain sense of reduced intensity occurred along the upper border. There was no recovery of touch, temperature or light

pressure sense. This flap was laid directly over bone in a field of considerable soft tissue scarring. The region of early pain recovery was comparatively free from scar.

CASE 9.—W. S. had an obliquely transposed flap on the medial side of the heel and ankle eleven years previously (fig. 11). Pain was present over the superior and anterior portions, while the posterior-inferior quadrant was totally insensi-

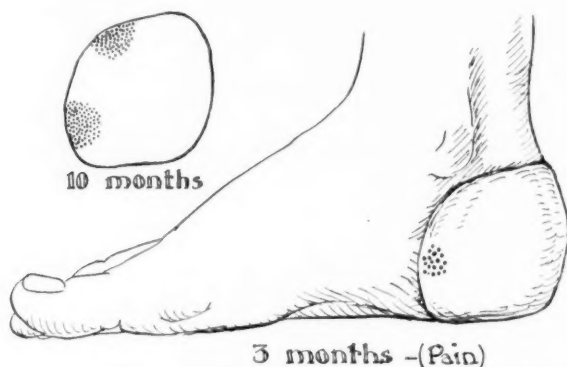


Fig. 10 (case 8).—Flap from thigh to heel. Small area of abnormal pain in three months.

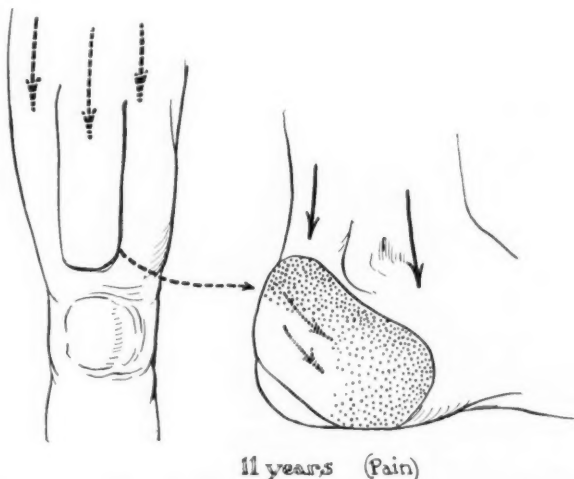


Fig. 11 (case 9).—Flap from thigh to heel. Polarity transverse. Incomplete recovery of pain after eleven years. No return of touch.

tive. Touch and temperature discrimination were absent. Why pain should recover over most of this flap and fail to return in a considerable area is difficult to explain. Deep scarring and attachment to bare bone probably prevented the ingress of new nerve fibers over the anesthetic area.

CASE 10.—L. G. presented various types of skin grafts applied three and a half years previously to cover defects resulting from severe burns. The entire dorsum of the right hand, including the bases of the digits, was covered by a large gauntlet

flap from the abdomen. Pain and light touch were normal over the entire flap. Response to cold at 20 C. was fairly accurate, while that to warmth at 45 C. was uncertain, particularly over the distal half (fig. 12). A large Wolfe graft above the ear showed a delayed response of diminished intensity to pin prick and cotton wool. Some appreciation of pain and possibly of touch was present over Thiersch grafts on the hand and scalp. As in other cases, Wolfe and Thiersch grafts showed much less recovery than the pedicle flap.

CASE 11.—M. N. presented a pedicle flap, 5 by 7 cm., from the abdomen to the dorsum of the hand. The polarity had been obliquely reversed. Examination after four years showed the response to pin prick, cotton wool and temperature differences to be quite normal.



3½ years - Warm Sensibility

Fig. 12 (case 10).—Flap from abdomen to dorsum of hand. Isopolar; complete recovery of pain and touch. Fair recovery of cold. Incomplete recovery of warm. Observed three and a half years after operation.

CASE 12.—B. S. presented long diamond-shaped Wolfe grafts over the third interdigital space of each hand. Examination after five years revealed a fair return of pain in both grafts, diminished touch in one, where little scarring was present, and a questionable return of temperature discrimination on the other.

CASE 13.—H. B., a woman, aged 52, had large areas over the leg covered with Thiersch and Reverdin grafts for stasis ulcers. The grafts ranged from ten to eighteen months in age. Examination revealed a diffusely spaced and incomplete recovery of pain in Thiersch grafts, a more complete recovery of pain in Reverdin grafts and a failure in return of touch and temperature in both.

CASE 14.—H. R., a woman, aged 58, presented a number of Reverdin grafts which had been applied six months previously over the region of the breast. Pain was present in about half the grafts, but none showed a return of touch.

CASE 15.—A. H., aged 33, presented Thiersch and Reverdin grafts that had been applied four years previously to cover a denuded area after radical amputation of the breast. Thiersch grafts showed small scattered areas of diminished response to pin prick, while most of the Reverdin grafts showed normal pain sensation. Touch and temperature discrimination were absent in both types of graft.

CASE 16.—I. L., presented two Thiersch grafts, 4 by 3 and 3 by 2 cm., transplanted to the lumbar region twelve years previously to cover a defect after excision of a chronically ulcerated roentgen burn. No return of cutaneous sensation had occurred because of deep scarring about and below the grafts.

CASE 17.—C. L. had a long tubed flap elevated over the back on the midscapular line for transplantation to the chin. The upper pedicle, the original attachment of which had been preserved for five months, showed an advance of pain area for a distance of 6 cm. from the base, while touch remained at 1 cm.

*Time in Months for First Detection of Pain, Touch and Temperature Sensation in Pedicle Flaps \**

Case	Pain	Touch	Temperature	Period of Observation	Polarity of Flap
1.....	6	10	18	18	Transverse
2.....	2½	7	8	9	Transverse
3A.....	5	8	16	20	Transverse
3B.....	5	6	9	12	Reversed
4.....	6	11	..	17	Reversed
5.....	3	..	..	3	Reversed
6.....	1-2	..	..	8	Transverse
7.....	..	..	..	15	Transverse
8.....	3	..	..	10	Transverse
9.....	132	..	..	132	Oblique
10.....	42	42	42	42	Isopolar
11.....	48	48	48	48	Oblique

\* Cases 9, 10 and 11 are late cases, and the patients were examined after a period of years.

CASE 18.—D. B. had a similar doubly pedunculated tubed flap elevated transversely over the back. The advance of pain in this case in five months was only from 2 to 2.5 cm., probably because of a moderate amount of scarring about the base.

#### COMMENT ON RESULTS

In our series of cases, recovery of sensation has been more complete in full-thickness pedicle flaps than in other types of skin transplants. The accompanying table shows the approximate time in months at which definite pain, touch and temperature were first detected in twelve pedicle flaps. Sensation was found to show first evidence of return as early as three weeks and to be incomplete as late as eleven years after transplantation. Only one flap, which was followed for fifteen months and was embedded in an area of dense cicatrix, has failed to show some evidence of recovery. Under favorable conditions, the pain area advances at an average rate of from 5 to 10 mm. per month.

In every case there has been a temporal dissociation in the return of the several modalities of sensation. The recovery has been in the order of pain, touch and finally temperature. According to Head's concept of protopathic sensation, the recognition of crude temperature dif-

ferences should have followed the recognition of pain, since it, too, is believed to depend on protopathic fibers. Touch, being subserved by epicritic fibers, should have appeared much later. That this does not occur is evidence against Head's concept. On the other hand, these findings in skin grafts lend no support to the critics of Head who deny all forms of temporal dissociation. Recovery of pain began in from two to six months and, under favorable conditions, was usually complete in nine months. The earliest return of light touch was in six months. Five flaps followed continuously have shown beginning return of touch at six, seven, eight, ten and eleven months. While some perception of cold seemed present in two flaps at eight and nine months, adequate temperature discrimination was found in but two cases and this at sixteen and eighteen months. Our findings are in disagreement with the statement of Davis and Traut that in skin grafts tactile sensibility recovers first. This difference may be due to the method of testing; theirs is not described. We have noted that contact with the head of a pin and heavy stroking with a camel's hair brush may be appreciated quite early. This response has been attributed to pressure and not to touch sensibility.

This temporal dissociation in the return of pain, touch and temperature sense is by no means proof of separate fiber systems. Boeke and Heringa have asserted that the explanation lies more probably in a differential rate for the development or reneurotization of end-organs in the skin. One would expect simpler nerve endings sensitive to pin prick to become functional before more complex ones subserving touch and temperature sense. In view of the lack of knowledge concerning the identity of the end-organs subserving the several types of cutaneous sensation, such deductions on data largely physiologic must remain speculative.

In two cases only has the early recovery of pain suggested hyperalgia or Head's protopathic pain. In both cases it was soon replaced by pain of normal or decreased intensity, which was properly localized. Sensation at a given point was first of diminished intensity and gradually became normal. In the few cases in which some temperature sense returned, perception was present only for wide differences and lagged far behind the return of light touch.

The point of first recovery of sensation has been about the periphery of a flap at the border of the proximal nerve supply. The area of recovery, when followed by repeated examinations, nearly always advances centrally and distally, with no apparent relation to the course of the original nerve fibers of the flap. Whatever the polarity of the flap, whether transverse or completely reversed, the recovery pattern progressed from proximal to distal and to some extent from the sides. One is led to wonder whether the old sheath cells played any appreciable rôle in the process of regeneration. In our type of material there is no ques-

tion of nerve suture or of any reapproximation of cut nerves. Fine cutaneous branches, after penetrating scar tissue, would have to find small bands of sheath cells in the transplant and follow a deviously retrograde course to larger branches in order to reach the center of a flap the polarity of which has been reversed. Also some branches, as in case 1, in which there was only marginal attachment of the flap, would end in central portions of the flap with no connections reaching the lateral borders where recovery of sensation first occurred. In that case there would be no opportunity for regeneration along sheath cells to the center unless extensive collateral anastomoses were assumed to exist. If cut fibers of the flap and bed should happen to become approximated, an opportunity for regeneration along some of the degenerated fibers would exist.

The completeness of recovery in many of the flaps is in marked contrast to the absence of incompleteness of return of sensation after division of large peripheral nerves. Possibly the smaller terminal branches of the cut borders of skin and subcutaneous tissue to which the flap becomes attached have the ability to send new fibers into a denervated field with little or no aid from its sheath cells. Speidel<sup>17</sup> has observed in the living tadpole regeneration of nerve fibers after traumatic degeneration without their being guided by either old or newly formed sheath cells. Whether or not this can occur in the human adult must be determined by direct anatomic evidence. Several of the flaps have been biopsied, and studies of the nerve fibers and endings will be reported subsequently.

The factors governing the rate and amount of sensory return in pedicle flaps are not entirely clear. In our series age has not seemed an important factor. When a flap is transplanted to an area where extensive scarring is present, recovery may be delayed or may not occur at all. Deep scarring at the border of a flap from infection or marginal necrosis during the process of implantation also retards the ingress of new nerve fibers, although superficial scarring of the skin does not. In three cases the flaps not only were partially surrounded by scar tissue, but were sutured directly over bone. Recovery in these cases was delayed, incomplete or, in some portions, entirely lacking. The gradual progression of the recovery pattern from the periphery in a number of cases suggests that ingress of new nerve fibers occurs largely in a plane more nearly parallel to the surface rather than from deeper structures. However, the absence of regeneration in two cases in which flaps were in contact with bone would suggest the interference of the latter with ingrowth of fibers from the floor of the defect. The recovery in case 1 was of necessity entirely by ingrowth from the sides. The latent period

17. Speidel, C. C.: *J. Exper. Zool.* **61**:279, 1932.

before any recovery of sensation can be elicited must be conditioned, in part at least, by the amount of scarring at the margins of a flap through which the regenerating fibers penetrate.

In three cases presenting Wolfe grafts, recovery of sensation was much less extensive and rapid than that of pedicle flaps. In case 4, with three interdigital grafts from the abdomen, some pain sense had returned in six months and touch in eighteen, while temperature remained absent. In case 10, a large Wolfe graft showed an incomplete return of pain and touch in three and a half years. Two grafts in case 11 showed, after five years, an incomplete recovery of pain, while touch was totally absent in one graft and subnormal in the other. The

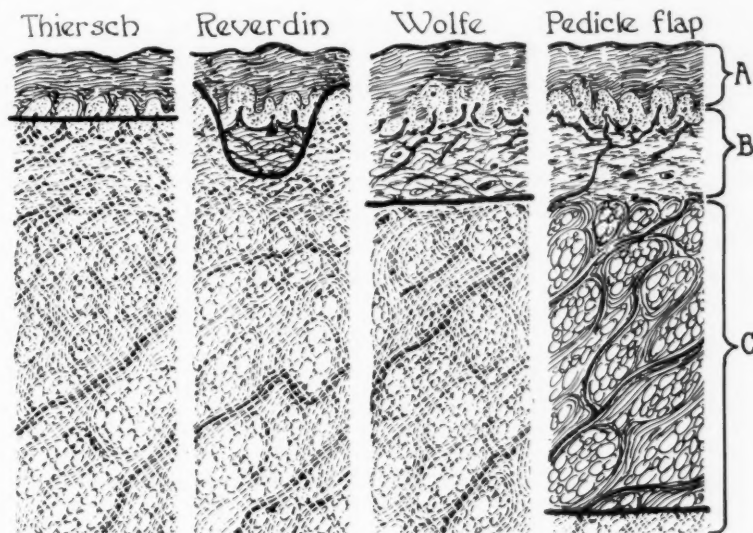


Fig. 13.—Cross-section of skin, showing depth of skin included in four types of skin transplants. *A* indicates the epidermis; *B*, the dermis; *C*, the tela subcutanea.

difficulty of testing temperature sense because of the size and position of these Wolfe grafts prevents any definite conclusions being drawn. But in all cases it was either markedly subnormal or absent.

The recovery of sensation in Reverdin grafts was found to be still less complete. In one patient some recovery of pain occurred in six months. In two cases there was good return of pain sense in nine and eleven months, while in two others recovery was incomplete in one and a half and four and a half years. We were unable to detect any recovery of touch or of temperature sense in our series of Reverdin grafts.

Thiersch grafts recovered less completely than the three other types. While some return of pain was evident in four cases in from eight to

eighteen months, the pain spots were infrequent and the intensity of sensation remained less than normal. Two patients showed no recovery in ten and twelve months. One presented diminished response to pin prick after three and a half years, while another patient showed but a few scattered areas of prick pain after four and a half years. In our series of ten patients with Thiersch grafts, no recovery of touch or of temperature discrimination occurred. We have found absence of recovery in the epithelial covering of a scar on the leg after thirty-four years.

The difference in the rate and amount of sensory return in the four types of skin transplants is marked and seems to depend on the thickness of the graft. Figure 13 shows schematically the amount of skin included in each type. The main horizontal course of the cutaneous nerve fibers is through the subcutaneous layer composed largely of fatty and loose areolar tissue. In pedicle flaps, regenerating fibers, after penetrating the scar at the border of the flap, can grow unimpeded through the subcutaneous layer and finally course superficially to their terminations in the dermis and epidermis. Since the blood supply of a pedicle flap is maintained throughout the course of transplantation, no necrosis or subsequent fibrosis occurs in the flap itself, and the only hindrance to the ingress of new nerves is at the border. In Wolfe grafts the subcutaneous layer is not included, so that regenerating nerve fibers meet with more or less extensive fibrosis at every point where they penetrate the dermis. In Reverdin and Thiersch grafts, which are composed largely of epidermis alone, fibrosis at the point of union of the graft with its bed seems to offer a marked barrier to the penetration of fine nerve fibers.

#### CONCLUSIONS

1. Varying degrees of recovery of cutaneous sensation occur in free and in pedicle skin grafts which have been totally denervated in the course of transplantation.
2. There is a temporal dissociation in the recovery of pain, touch and temperature sensation in all types of grafts.
3. In pedicle flaps, under favorable conditions, pain begins to return in from three to six months and is usually complete within a year. Touch returns in from nine months to a year, and may be complete. In cases unfavorable for ingrowth it may be slight or altogether absent. Temperature discrimination for wide differences lags behind the return of touch, but in some cases is fairly extensive.
4. Recovery of sensation in pedicle flaps usually begins about the periphery, at the point of proximal nerve supply, and progresses distally and from the sides.
5. There is apparently no relation between the course of the original neurilemmal sheaths of a flap and the ingress of new nerve fibers. The

recovery pattern supplied no evidence of restoration of sensation corresponding to branches of nerves contained in the flap. On the contrary, some cases presented strong physiologic evidence that cut nerves of the bed invade a flap independently of the old neurilemmal sheaths.

6. Regeneration of sympathetic control of sudoriferous glands occurs late. Partial recovery of sweating has been observed in two cases in from a year to a year and a half.

7. Deep cicatrization of tissues at the border of a flap or a bed of bone makes an unfavorable field for the invasion of new nerve fibers.

8. Recovery of sensation is more rapid and more complete in pedicle flaps than in Wolfe, Reverdin and Thiersch grafts. The difference in recovery may be explained by the location of the barrier presented by scar tissue at the point of union of a graft with its bed and by the amount of degeneration and fibrosis from disturbance of the blood supply during transplantation.

#### SUMMARY

Recovery of cutaneous sensation is described in a series of full-thickness pedicle flaps and free skin transplants. The recovery pattern gives no evidence that regenerating nerve fibers in the skin follow old neurilemmal sheaths. Recovery took place in varying degrees and was greatest in pedicle flaps, followed in order by Wolfe, Reverdin and Thiersch grafts. Pain sensation invariably recovers first, while touch is second and temperature discrimination last.

# INTRACRANIAL HYDRODYNAMICS

## I. EXPERIMENTS ON HUMAN CADAVERS

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It is our purpose in this series of papers to present the results of experiments designed to reinvestigate certain aspects of the related subjects of intracranial hydrodynamics and cerebral edema. The work was prompted by the disagreement that seems to exist in the past and current literature with regard to such important questions as the relative dangers of ventricular and lumbar punctures, the etiology of untoward effects following rachicentesis, the causes of "herniation" of the brain stem and other topics that are necessarily related to our subject.

The present paper deals with the method evolved for investigating intracranial hydrodynamics in fresh human cadavers. The second communication will describe a series of animal experiments on the possible hydrodynamic etiology of edema of the brain. The third article will present a résumé of the extensive literature, report certain original experimental and clinical data and attempt a correlation of our findings with those of other authors, as described in their publications during the past hundred years.

### METHOD

*Material.*—Bodies were obtained as soon as possible after death—always within two hours. The initial step in their preparation consisted in the bilateral ligation of the jugular, carotid and vertebral veins, the cerebral circulation being thus almost completely isolated. A trocar was then tied into either jugular vein, and the cerebral venous pressure was maintained at any desired level by means of physiologic solution of sodium chloride from a pneumatic bottle (fig. 1). Trephine openings were made over the occipital regions of the skull, and the holes were tightly closed by truncated rubber corks. Through these, large bore needles were inserted into the occipital horn of each lateral ventricle. Similar needles were then inserted into the cisterna basalis and into the lumbar subarachnoid sac of the cord, respectively. Each needle communicated with its individual manometer through a two-way stopcock. The ventricular needles, in addition, were connected with a reservoir of radiopaque solution, so mounted as to be adjustable to any desired height.

*Solution Used.*—The radiopaque solution employed was adopted only after an investigation of about thirty others. Various concentrations of lead, bismuth, barium and iodide salts, several iodized oils and a number of emulsions of the latter were tested for radiopacity, viscosity, diffusibility and fixing effects on nerve tissue (fig. 2 and table). Iodized poppy-seed oil, 40 per cent, iodized rape-seed oil emul-

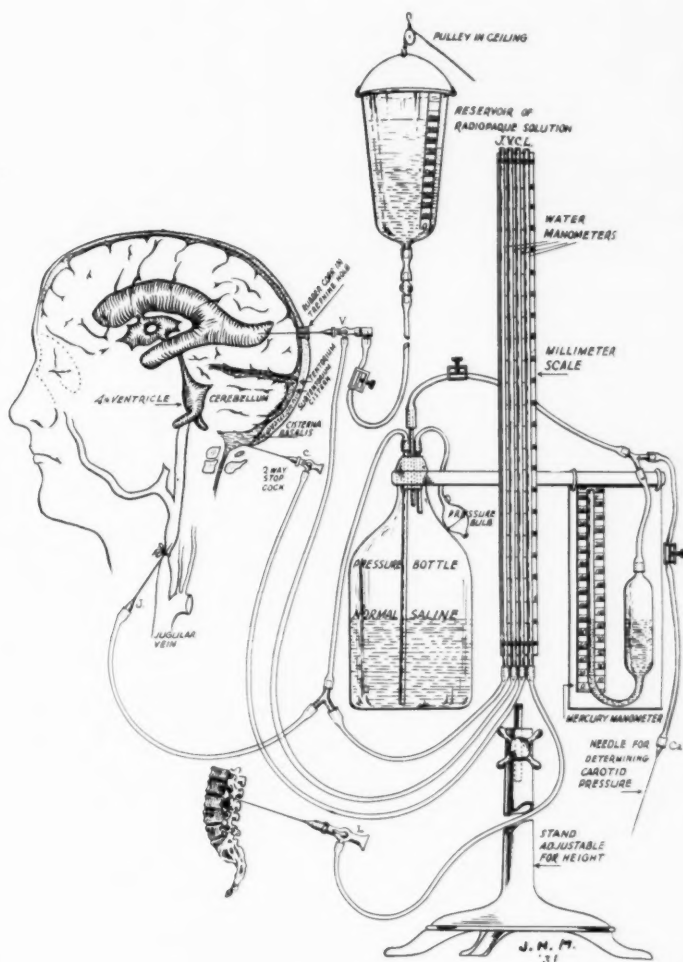


Fig. 1.—Apparatus for investigating the hydrodynamics of the ventriculosubarachnoid system. Needles *V*, *C* and *L* are large-bore lumbar puncture needles inserted into the lateral ventricle, basal cistern and lumbar subarachnoid sac respectively. Each needle is connected, through a two-way stopcock, to its corresponding small-bore glass manometer (*V*, *C*, *L*). In addition, the ventricular needle is connected to an adjustable graduated reservoir of radiopaque solution.

Needle *J* is tied into the jugular vein and connected with a pressure bottle containing physiologic solution of sodium chloride. By manipulation of the illustrated pinch-cocks, pressure values in this system may be read as indicated, either in water or in mercury.

All four water manometers are mounted on an adjustable upright stand so that their zero points may be lowered to the horizontal level of the subject's spine.

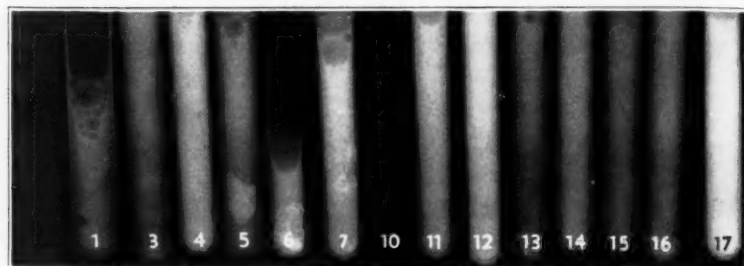


Fig. 2.—Comparative radiopacity of the solutions numbered and described in the table.

*Effect of Various Radiopaque Solutions on Nerve Tissues*

Solution No.	Substance	Viscosity at 20 C. as Compared with Water		Radiopacity	½ Hour	2 Hours	6 Hours	48 Hours
		Per Cent						
1	Barium acetate	10	1.0	***	No definite effect	No definite effect	Slightly softer; pliable	Slightly softer; unmacerated
2	Barium acetate	15	1.0	****	No definite effect	No definite effect	Slightly softer; pliable	Slightly softer; unmacerated
3	Barium chloride	10	1.0	***	No definite effect	Same	Slightly softer	Slightly softer; elastic; unmacerated
4	Barium chloride*	15	1.0	****	No definite effect	Same	Slightly softer	Slightly softer; elastic; unmacerated
6	Lead acetate	10	1.0	***	Slightly firmer	Same	Granular	Firm; inelastic; gritty
7	Lead acetate 5% with acacia 5%	..	1.3	**	No definite effect	Slightly firmer	Granular but elastic	Granulated; unmacerated
11	Sodium iodide	15	1.0	****	No definite effect	Slightly softer	Softer	Semigelatinous; translucent
13	Lead acetate with acacia	10 5	1.3	***	Slightly firmer	Same	Slightly granular	Granular; elastic
14	Lead acetate	5	1.0	**	No definite effect	Firmer; slightly granular	Same	Firm; granular
15	Barium acetate with acacia	10 5	1.3	***	No definite effect	No definite effect	No definite effect	Slightly softer
17	Sodium iodide with acacia	15 5	1.3	****	No definite effect	No definite effect	Softer	Elastic; semitranslucent

\* Barium chloride successfully fulfilled the experimental requirements.

sion and other nondiffusible iodized oil products<sup>1</sup> gave crystal-clear roentgenographic definition, but the relatively high viscosity of these preparations rendered the reading of intracranial pressures inaccurate. Solutions of lead salts fixed the nerve tissues, whereas the alkaline iodides, even with the addition of acacia, diffused too rapidly and would fog encephalograms taken late in the experiment. Fifteen per cent barium chloride, however (table, solution 4), proved less diffusible, in keeping with the lower position of its anion in the so-called Hofmeister series.<sup>2</sup> Also, the salt had no tendency to harden the tissues; the viscosity of its solution was practically that of cerebrospinal fluid, and it gave roentgenograms of the ventriculosubarachnoid system of sufficient clarity to enable accurate comparative measurement of series of plates to be made.

For convenience, the radiopaque solution was tinted with a small quantity of gentian violet, so that colorimetric comparisons could be made between the fluid drained from any of the needles and the original solution contained in the reservoir.

*Procedure.*—At the beginning of an experiment, the cadaver was placed in a horizontal plane, and its head was fixed over the center of a rotary Bucky diaphragm in such a posture as to center the occipital region beneath the Coolidge tube of an x-ray apparatus. The positions of the tube, head and Bucky diaphragm remained unchanged throughout the experiment, so that serial encephalograms were in every way comparable.

In our earlier work, we maintained a constant pressure of 20 mm. of mercury in the venous pneumatic bottle system throughout each experiment, empirically adopting this figure as the one most likely to compensate for the postmortem loss of both the venous and the arterial intracranial pressures. Later, we varied the venous pressure so as to maintain it at 50 cm. of water above that of the fluid in the subarachnoid space, with the idea of preventing both collapse and overdilatation of the intracranial venous bed. This variation in procedure, however, appeared to make no difference in the charted results.

Manometry was begun by adjusting the tube stand so that its zero point was on a horizontal level with the subject's spine. The reservoir was then raised until the surface of its contained fluid was 20 cm. above the base line. With the lumbar needle closed and the cisternal needle open, the radiopaque solution was allowed to flow into the ventricles until the first tint of color appeared in the fluid draining from the cistern—an interval of from one hundred and twenty to two hundred and sixty seconds. The cisternal needle was then closed and fluid was drained from the lumbar one. Color usually appeared in the lumbar fluid in about another minute and, in an additional four minutes, grew intense enough to indicate that the subarachnoid spaces between ventricles and lumbar spine were filled with solution of adequate radiopacity. At this point, a "normal" encephalogram was taken, the typical appearance of which is illustrated in figure 3.

1. Sicard, J. A., and Forestier, J.: Roentgenologic Exploration of the Central Nervous System with Iodized Oil, *Arch. Neurol. & Psychiat.* **16**:420 (Oct.) 1926. Raiziss, G. W.; Glaser, M., and Clemence, LeR. W.: Chemistry in Application of Campidol (Iodized Rapeseed Oil) in Roentgenography, *J. Lab. & Clin. Med.* **16**:943, 1931.

2. Alexander, J.: Colloid Chemistry, New York, The Chemical Catalogue Company, Inc., 1926, vol. 2, p. 423.

With the intraventricular, cisternal and lumbar pressures at 20 cm. (values are in columns of water), the reservoir was shut off from the ventricular needles. The lumbar cock was then opened and 10 cc. of fluid allowed to drain off, while the readings of the ventricular and cisternal manometers were noted at five second intervals. At the end of this first "lumbar tap," the lumbar needle was closed and another encephalogram taken for comparison with the first. The subarachnoid pressure was then restored to 20 cm. with solution from the reservoir, and fluid was drained from the cisternal needle, the lumbar and ventricular manometers being read at five second intervals. At the end of the cisternal tap, the third encephalogram was taken, completing the 20 cm. series.

Next, the reservoir fluid level was raised to the 50 cm. base line, the subarachnoid pressure thus being increased to 50 cm. throughout. The reservoir was then shut off, and the lumbar and cisternal drainages were repeated seriatim, manometric readings once again being recorded during, and encephalograms taken following,

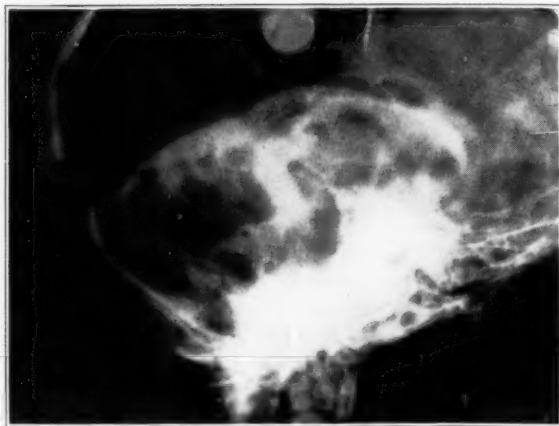


Fig. 3.—"Normal" encephalogram. Intraventricular pressure of 20 cm. of water. Technic: 8 kilovolts; 20 milliamperes; 30 inches (76.2 cm.); 5 seconds; rotary Bucky diaphragm. The tentorial ridge, subtentorial cistern, fourth ventricle, cerebellar tonsils and basal cistern are outlined. The ventricular and cisternal needles may be seen in situ.

each of the taps. Finally, the entire procedure was repeated for initial pressures of 80 cm. of water, this value approximating the pathologic maximum found during life.

At the conclusion of each experiment, the brain was removed for gross and microscopic section. The results recorded in this paper are those of eight experiments on subjects whose central nervous systems were thus determined to have been grossly normal.

*Comment.*—By the procedure outlined we attempted, in effect, to:

1. Obtain roentgenograms of the ventriculosubarachnoid system under various degrees of fluid pressure.
2. Determine possible movement of the cerebellum or medulla when various intraventricular fluid pressures were released through cisternal or lumbar tap.

3. Investigate the hydrodynamic effect of each drainage on fluid pressures in other portions of the ventriculosubarachnoid system.

Cadavers necessarily were used, as the only method of pursuing even the roentgenologic part of this investigation clinically would be to inject a preparation of iodized poppy-seed oil into the basal cistern of a patient with a high cerebrospinal fluid pressure, take a control encephalogram and repeat the roentgen examination after rapid lumbar tap to determine possible cerebellar or medullary movement. Such a procedure would be interesting, but also, according to our present conception of intracranial hydrodynamics, potentially dangerous.

Ayer<sup>3</sup> analyzed the possible factors concerned with regulation of the spinal fluid pressure, as follows:

1. Hydrostatic pressure, provided the patient is in any position other than the horizontal.
2. Brain bulk, or the amount of solid substance within the cranium.
3. The secretion pressure of the cerebrospinal fluid.
4. The rate of absorption of the fluid.
5. The elasticity of the dura mater.
6. Intracranial arterial pressure.
7. Intracranial venous pressure.

Factors 1 and 2 are fulfilled in the procedure of our experiments. Factors 3 and 4 are obviously not involved in the effects of rapid movements of cerebrospinal fluid with which we are concerned. With regard to factor 5, Weed,<sup>4</sup> in discussing the Monro-Kellie hypothesis, concluded that the dural tube of live mammals may be considered as fairly, though not absolutely, rigid. His findings, therefore, discount the importance of any hypothetical stiffening of the meninges that may have occurred in our experiments. As to other possible postmortem alterations, the predominant changes in the consistency of brain tissue after death are those of swelling and softening, processes that would favor, rather than hinder, subsequent cerebellar or medullary descent under fluid pressure from above. The absence of any such movements in the brain stem in our experiments would, therefore, be especially significant.

Factors 6 and 7 presented greater difficulties, and the remaining criticism of the method must be formulated on the basis that the intracranial vascular pressures had not been satisfactorily approximated. True, the jugular pneumatic bottle is obviously inadequate in restoring

3. Ayer, J. B.: Cerebrospinal Fluid Pressures from the Clinical Point of View, Association for Research in Nervous and Mental Diseases, New York, Paul B. Hoeber, Inc., 1926, vol. 4, p. 159.

4. Weed, L. H.: Some Limitations of the Monro-Kellie Hypothesis, *Arch. Surg.* **18**:1049 (April) 1929.

vital intracranial arterial pressure, venous and respiratory variation, etc. Nevertheless, the relatively small loss of saline solution from the bottle (80 to 20 cc. in a period of one to two hours) indicates fairly efficient preliminary ligation of the intracranial vascular system and, therefore, fairly complete retention of the original intracranial blood volume, which, according to Hill,<sup>5</sup> varies little in any case. Again, were cerebellar herniation due to sudden subtentorial venous engorgement, the comparatively high pressures in our pneumatic jugular system (fig. 1) would favor, rather than hinder, such an occurrence. It may be relevantly noted, also, that the pressure effects of the venous bed of the cord, possible collapse of which may have occurred in our experiments, are considered by Weed<sup>4</sup> to be of minor importance.

It may be seen, then, that even if the complete restoration of lifelike circulatory conditions is practically impossible, our experiments fulfilled, in the main, the vital factors of intracranial hydrodynamics. Our findings, therefore, may, within certain limits, be held to be valid for the living.

#### INTERPRETATION OF PRESSURE READINGS

Figure 4 illustrates the fall of intraventricular and intracisternal pressures from various initial levels during rapid spinal drainage of 10 and 20 cc. of fluid. The respective readings are, in general found to be parallel, even when intraventricular pressures of over 75 cm. are rapidly released through lumbar tap. Significantly, neither the ventricular nor the cisternal pressure curves show any tendency to a plateau effect, such as might result from a block at the foramen magnum through medullary or cerebellar herniation.

Figure 5 records the ventricular and lumbar curves of pressure during cisternal drainage, and shows the two hydrodynamic extremes of the ventriculosubarachnoid system to be in fairly open communication. The curves are parallel, and there is again no evidence of foraminal block, even on sudden cisternal release of high intrathecal pressures. This agrees well with the findings of Ayer,<sup>6</sup> who showed that in human beings cisternal and lumbar pressures remained parallel on deep inspiration, jugular compression, crying, etc., and concluded that "normally, the spinal subarachnoid space permits free passage of fluid in either direction." Ayer quoted Purves-Stewart as having obtained a like correspondence between horizontal ventricular and lumbar pressures, and Cushing<sup>7</sup> reported similar observations on children. F. L. Reichert, in a personal communication, also cited a relevant instance in which,

5. Hill, Leonard: *Physiology and Pathology of Cerebral Circulation*, London, J. & A. Churchill, 1896.

6. Ayer, J. B.: Spinal Subarachnoid Block as Determined by Combined Cistern and Lumbar Punctures, with Special Reference to Early Diagnosis of Cord Lesions, *Arch. Neurol. & Psychiat.* **7**:38 (Jan.) 1922.

7. Cushing, Harvey: *Studies in Intracranial Physiology and Surgery*, London, Oxford University Press, 1925.

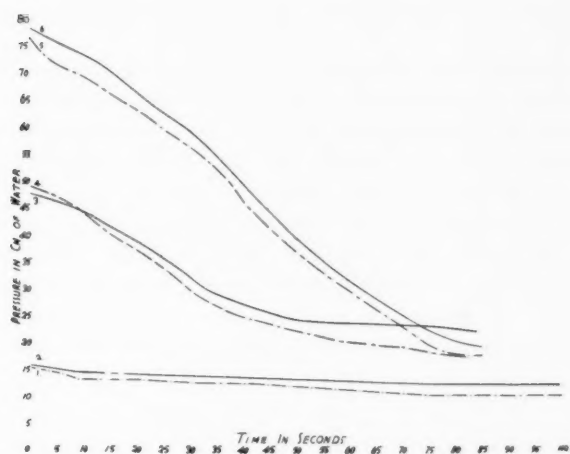


Fig. 4.—The curves of intraventricular (solid line) and intracisternal (broken line) pressures during removal of fluid by lumbar tap run parallel. Curves 1 and 2: 10 cc. of fluid removed in one hundred seconds. Curves 3 and 4: 20 cc. removed in eighty-four seconds. Curves 5 and 6: 20 cc. removed in eighty-five seconds. An occasional lag in the higher readings is entirely attributable to mechanical stasis consequent on the relatively small bore of the valves or needles. The absence of plateau effect in the ventricular or cisternal pressures, even on sudden release below, indicates that no block occurred at the foramen magnum under those conditions.

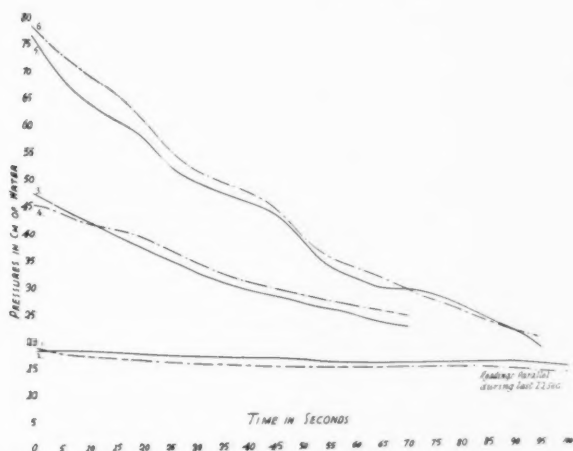


Fig. 5.—Parallel pressure readings at the two extremes of the ventriculo-subarachnoid system during removal of fluid by cisternal tap indicate free fluid communication between both loci and the point of cisternal drainage (intraventricular pressure, solid line; lumbar pressure, broken line). Curves 1 and 2: 10 cc. of fluid removed in one hundred and twelve seconds. Curves 3 and 4: 20 cc. removed in seventy seconds. Curves 5 and 6: 20 cc. removed in ninety-five seconds. The absence of plateau effect in the lumbar curve indicates the absence of foraminal block, even on sudden release of the higher ventricular pressures by cisternal tap.

preceding a craniotomy on a patient with a tumor of the brain, he had occasion to insert ventricular, cisternal and lumbar needles. Reichert noted that the horizontal pressure readings at the three loci remained equal under various manipulations. Similar observations have been reported by a number of other authors.<sup>8</sup>

We may, therefore, infer that even relatively sudden and large variations of pressure are, under normal conditions, fairly well transmitted from one portion of the ventriculosubarachnoid system to another.

#### INTERPRETATION OF ROENTGENOGRAPHIC FINDINGS

Figure 3 illustrates the usual appearance of the tentorium, subtentorial cistern, fourth ventricle, cerebellar tonsils and basal cistern in the control encephalogram taken at the beginning of each experiment. It was anticipated that movement of the cerebellum in subsequent plates would be indicated by widening of the subtentorial cistern, lowering of the cerebellar tonsils and partial or complete obliteration of the cisterna basalis, whereas descent of the medulla would be indicated by a change in the shape or position of the fourth ventricle. Later encephalograms, however, when compared with the control by superposition or careful mensuration, show no displacement or distortion of either the tentorium or any of the subtentorial structures. This immobility of the cerebellum and medulla held true even after sudden lumbar release of high intraventricular pressures. The findings agree well with the concomitant lack of fluid block as measured manometrically under these circumstances, and with the absence of cerebellar descent on final gross inspection of the brain.

In effect, neither the plates nor the pressure charts revealed any evidence of cerebellar or medullary "herniation" under conditions that would most favor such an occurrence.

#### TUMORS

In three experiments, attempts were made to study the mechanical effects of tumors in various regions on intracranial hydrodynamics. "Tumors" were produced by the injection of melted paraffin, from 20 to 40 cc. of which was allowed to solidify in various regions inside the skull. Distortions so produced in the frontal or occipital cerebral regions had no apparent effect on the fall of ventricular or cisternal pressure curves when fluid was removed by lumbar tap. However, when 30 cc. of wax was injected into the left cerebellar lobe, a partial block between

8. Dandy, W. E., and Blackfan, K. D.: An Experimental and Clinical Study of Internal Hydrocephalus, *J. A. M. A.* **61**:2216 (Dec. 20) 1913. Dahlstrom, S., and Wideroe, S.: *Ztschr. f. d. ges. Neurol. u. Psychiat.* **72**:75, 1921. Solomon, H. C.; Thompson, L. J., and Pfeiffer, H. M.: Circulation of Phenolsulphonphthalein in the Cerebrospinal System, *J. A. M. A.* **129**:1014 (Sept. 23) 1922. Ruggles, A. H.: Observations in Ventricle and Cistern Punctures, *Arch. Neurol. & Psychiat.* **11**:227 (Feb.) 1924. Cushing, H.: *Lancet* **2**:851, 1925.

ventricular and lumbar spaces was effected. Subsequent examination showed the paraffin to have forced the left cerebellar lobe down against the bulb, partially obliterating the fourth ventricle and basal cistern. It is of interest to compare these observations with the findings of Fremont-Smith and Hodgson,<sup>9</sup> who performed combined ventricular and lumbar puncture in twenty-one cases and concluded: "In patients with subtentorial tumors, some degree of block between the lateral ventricle and the lumbar subarachnoid space may be expected. No such block has been found when the tumor lies above the tentorium."

Of interest, too, is the fact that the encephalogram, even in the last quoted instance, revealed no elevation of the tentorium, although the subtentorial pressure must have been greatly increased by the injection of paraffin. This finding agrees with the views of Dandy,<sup>10</sup> Crothers,<sup>11</sup> Krause<sup>12</sup> and others, as to the relative immobility of the tentorium, a topic on which we shall have occasion to comment in a later paper.

#### SUMMARY

A method of investigating craniovertebral hydrodynamics in fresh human cadavers is presented.

Our experimental results were:

1. The lateral ventricles and the cisternal and lumbar subarachnoid spaces remained in free communication under all experimental variations in pressure, provided no distortion of the subtentorial structures was artificially produced.
2. In the absence of such distortion there was no evidence of tentorial, medullary or cerebellar movements under any experimental variations in subarachnoid fluid pressure.
3. Distention of the frontal or occipital lobes of the cerebrum by the injection of from 20 to 40 cc. of melted paraffin produced no demonstrable interruption in free fluid communication between the lateral ventricles and lumbar sac.
4. The injection of 30 cc. of paraffin into the left cerebellar lobe forced it down against the medulla and caused a partial hydrodynamic block between the lateral ventricles and lumbar sac.
5. No demonstrable movement of the tentorium occurred under any of our experimental variations of intracranial pressure.

9. Fremont-Smith, F., and Hodgson, J. S.: Combined Ventricular and Lumbar Puncture, Association for Research in Nervous and Mental Diseases, New York, Paul B. Hoeber, Inc., 1926, vol. 4, p. 172.

10. Dandy, W. E.: The Space Compensating Function of the Cerebral Fluid, *Bull. Johns Hopkins Hosp.* **34**:245 (Aug.) 1923.

11. Crothers, B.: Changes of Pressure Inside of Cranio-Vertebral Cavity, *Surg., Gynec. & Obst.* **37**:740 (Dec.) 1923.

12. Krause, F.: *Surgery of the Brain and Spinal Cord*, translated by H. A. Haubold, New York, Rebman Company, 1909, vol. 1.

## DIFFUSE SCLEROSIS WITH PRESERVED MYELIN ISLANDS

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Among different diseases of the brain which are characterized by demyelination of the white matter and which are mostly designated diffuse sclerosis, is one shown in a small group of four observations in which islands of preserved myelin have been reported. This type of demyelination was described for the first time by Merzbacher<sup>1</sup> in a child in whose family a peculiar hereditary disease of the brain had occurred in several generations. A second case from the same family was published by Spielmeier and Liebers<sup>2</sup> and, further, there are two sporadic observations, one by Bielschowsky and Henneberg<sup>3</sup> and one by Bodechtel.<sup>4</sup>

This condition is patho-anatomically characterized by a peculiar degeneration of the white matter of both hemispheres of the brain and that of the cerebellum, the pons, the medulla and even the spinal cord. Within the destroyed areas there remain numerous perivascular myelin islands, so that the destruction of the white matter is not complete.

In this article we present the clinical and anatomic findings in a further case which is patho-anatomically and histologically identical with the observations mentioned, but shows few similar clinical trends.

### REPORT OF A CASE

*Clinical History.*—F. S., aged 54, married, a common laborer, was admitted to the outpatient clinic of the University of Michigan Hospital on Sept. 4, 1928, complaining of stiffness and difficulty in the use of his extremities, pains in the back,

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From the State Psychopathic Hospital, Ann Arbor, Mich., and the Traverse City State Hospital, Traverse City, Mich.

1. Merzbacher, L.: Eine eigenartige familiär-hereditäre Erkrankungsform, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **3:1**, 1910.

2. Liebers, Max: Zur Histopathologie des zweiten Falles von Pelizaeus-Merzbacherschen Krankheit, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **115:487**, 1928.

3. Bielschowsky, M., and Henneberg, R.: Ueber familiäre diffuse Sklerose (Leukodystrophia cerebri progressiva hereditaria), *J. f. Psychol. u. Neurol.* **36:131**, 1928.

4. Bodechtel, Gustav: Zur Frage der Pelizaeus-Merzbacherschen Krankheit, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **121:487**, 1929.

occasional loss of control of the bladder and burning sensation on urination. The first symptoms appeared in 1917, at the age of 43, when it was observed that he was slower in movements and had developed a shaking of the right arm. He later experienced difficulty in walking, a sense of stiffness in the extremities and periods when he would fall and be unable to rise. The last symptom first appeared in 1924, and recurred at infrequent intervals for three years. Thereafter, the periods of falling occurred more frequently. During the attacks, the head drew to the right, and the patient was unable to talk, but would crawl about the floor helplessly until assisted. After a few hours of rest he would recover fully. Headaches, though not a prominent symptom, were present. The family history was unimportant.

*Examination.*—The patient was of pyknic habitus and well nourished. There were no deformities. The heart and lungs were normal. The blood pressure was 135 systolic and 80 diastolic. There was a moderate degree of sclerosis of the peripheral vessels. Abdominal examination gave negative results. The spine was normal.

On neurologic examination, comprehension and orientation were found to be normal. There was definite impairment of memory. In speech, the patient showed difficulty in articulating, and there were some slurring and elision of syllables. He walked with a somewhat stiff gait, with no ataxia with the eyes open, but with some unsteadiness when they were closed. In the Romberg position he swayed slightly. There were coarse, irregular tremors of the extended fingers and an intention tremor of the right hand. In the test for adiadokokinesis he was awkward. There were no localized or generalized muscular atrophies. The pupils were constricted and regular, but reacted with some sluggishness both to light and in accommodation. There was no nystagmus. The cranial nerves were normal. All deep tendon reflexes were slightly increased, equally on the two sides. The umbilical reflexes were present. There was no Babinski sign. The sense of motion and position and vibratory sense were preserved in the upper and lower extremities.

*Laboratory Studies.*—The Kahn reaction of the blood was negative. The cerebrospinal fluid was normal. The urine contained a trace of albumin.

*Course.*—Four subsequent examinations were made. On Oct. 29, 1928, the findings were essentially the same. On July 9, 1929, the patient stated that he felt somewhat better, but complained of generalized weakness. The neurologic signs, however, were essentially unaltered. On October 2, there was a distinct intention tremor of both arms, with ataxia of the right arm. This extremity he held in a flexed posture, with the fingers flexed and the hand in a strained position. On October 16, he complained of an aching pain in the right flank. On examination, there were found: limitation in outward rotation of the eyeballs; a constant rhythmic tremor of the right hand; increase in the tonus of all muscles of the extremities; occasional intention tremor of the head; marked intention tremor of the upper extremities; generalized hyperreflexia; a suggestive scanning quality to the speech; a positive Babinski sign on the right and a suggestive one on the left, and abortive ankle clonus bilaterally, which was more marked on the right. Sensory tests showed that sensation was intact. The fundi were normal. Visual acuity was 5/12 in both eyes with correction. A dental examination with roentgen studies of the teeth showed no foci.

When the patient was first seen in 1928, the diagnosis made by one of us (T. S. H.) was a diffuse degenerative lesion of the central nervous system. Subsequent examiners considered the case to be multiple sclerosis.

In the latter part of 1929, there occurred a progressive intellectual deterioration. There were periods of confusion, but no definite loss of consciousness or convulsive seizures. The gait became more unsteady, and the patient fell frequently. On Dec. 13, 1929, while carrying some coal, he fell suddenly and was unable to rise without help. He talked in a confused manner immediately thereafter, but was unable to speak on the following day or to recognize relatives. After a week's confinement to bed he was able to walk again, but was much worse than previously. The right arm shook continuously, and he was scarcely able to eat or to dress himself. He complained of dizziness, headaches and insomnia. At night he would rise four or five times and wander about the house.

The patient became increasingly erotic, and would kiss, exhibit himself before and carry on an imagined discourse with pictures of women. He was admitted to the Traverse City State Hospital on Dec. 9, 1930.

*Examination at Traverse City State Hospital.*—The neurologic picture was essentially as already reported.

On psychiatric examination, the patient was found to be generally euphoric, restless, overtalkative and often emotionally unstable, and he lacked insight into his mental state. When engaged in conversation he endeavored to attend and comprehended all questions. He was at times oriented, but again would be grossly disoriented, both temporally and spatially; difficulty in recall and retentive memory was present. He frequently contradicted himself and showed defective judgment. At times, he would admit his former erotic interests but believed them normal, and again he would deny them. In his paranoid ideas, he believed that his wife was jealous of him and wished him placed out of the way; his sister bore him a grudge and was also responsible for his incarceration. He claimed that arsenic had been placed in his food. There were no hallucinations.

The course in this hospital was characterized by a gradually increasing deterioration, with periods of confusion, an increase in the pyramidal tract signs and tremors, and faulty coordination. The patient experienced dizzy spells during which he would at times fall. On March 12, 1931, lobar pneumonia developed, and he died six days later.

*Summary.*—A man, aged 54, whose family history was unimportant, had become ill at 43 with stiffness and pain in the back, loss of control of the bladder and difficulty in walking. There were: difficulty in articulation; stiff gait, but no ataxia; irregular tremor of the fingers, and intention tremor of the right hand. The cranial nerves were normal, the tendon reflexes slightly increased, and serologic tests negative. One year later there were distinct tremor of both arms and ataxia of the right arm, with increased tonus of all muscles of the extremities, marked intention tremor of the upper extremities, generalized hyperreflexia and a positive Babinski sign on the right. The gait was more unsteady, and the patient was frequently dizzy. There was progressive intellectual deterioration with periods of confusion. He became increasingly erotic, and an organic mental syndrome, with mild paranoid trends, developed. He died on March 18, 1931, of lobar pneumonia after an illness of approximately eleven years.

*Anatomic Description.*—The leptomeninges were somewhat cloudy over both convexities; the basal vessels were normal. The convolutions were atrophic, especially over both frontal and parietal lobes. The pons, medulla and cerebellum presented normal outlines. The weight of the brain was 1,100 Gm.

Horizontal sections through the brain showed: The gray matter of the cortex was of normal width and outline, atrophy of the convolutions being brought about by a peculiar destruction of the white matter. The latter was greatly shrunken (figs. 1 and 2) and of a smoke gray appearance, and in places also somewhat bluish gray. The myelin was nowhere entirely destroyed, and there remained

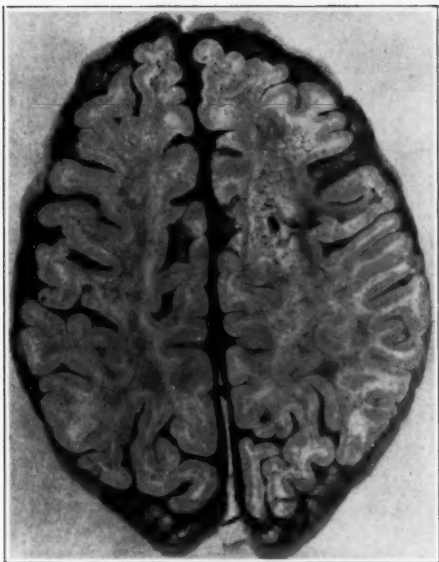


Fig. 1.—Frontal section through both hemispheres above the ventricles. The gray matter is entirely preserved. The U fibers are mostly preserved. Part of the white matter in the convolutional crests is still visible. There are multiple islands of white matter in both hemispheres.



Fig. 2.—Horizontal section through both hemispheres and the basal ganglia. Hydrocephalus ex vacuo. The internal capsule and basal ganglia are well preserved; otherwise, the same picture as in figure 1.

countless white islands of preserved white matter. The size of these islands varied considerably. There were many the size of a pinhead and smaller; others, again, were the size of a lentil and larger (figs. 1 and 2). All layers of the white matter, superficial as well as deep, and those of the convolutional crests were affected, but the intensity of the destruction was not uniform; the convolutional crests and the U fibers were frequently preserved. No fiber system was preferred; on the other hand, none was spared. On the whole, the frontal lobes were more damaged than the occipital lobes, but the difference was not impressive.

In horizontal sections through the ventricles and basal ganglia, the atrophy of the white matter was particularly well seen (fig. 2). The caudate nucleus, putamen, pallidum and external and internal capsules were preserved and distinctly outlined. There were several small gray foci in the corpus callosum.

The lateral and third ventricles were considerably enlarged as a result of the demyelination (hydrocephalus ex vacuo, fig. 2).

The thalamus, subthalamic region, pons, medulla, cerebellum and spinal cord were without gross changes.

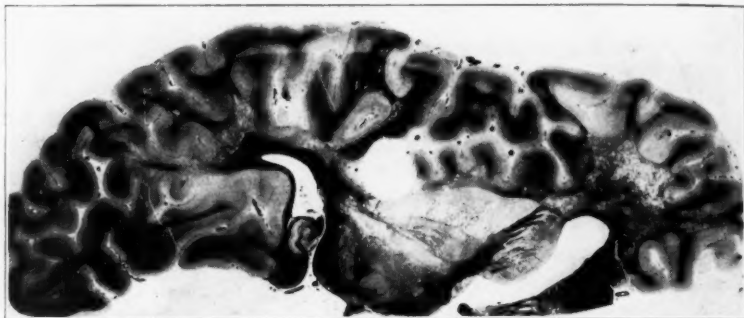


Fig. 3.—Diffuse degeneration of the white matter, pallidum and thalamus. There are slight disturbances of the cortex and the U fibers. Weigert-Kultschitzky stain.

The fourth ventricle was not enlarged.

Weigert sections revealed certain additional points: On the whole, they confirmed the findings of the macroscopic examination of unstained blocks, but proved at the same time that the gray matter was not entirely free from changes; several restricted areas of demyelination were present in the insula and in the parieto-occipital lobes; otherwise, the myelo-architecture was normal (figs. 3, 5 and 6). The peculiar patchy distribution of the demyelination was extremely well demonstrated in these preparations (fig. 3).

*Histologic Examination.*—The meninges were normal. The cyto-architecture of the cortex (Nissl sections) was fully preserved, and the cells showed only slight unspecific changes (fig. 4). Sudan sections revealed considerable amounts of fat in the parenchymal elements. With the exception of very few and scattered fixed glial elements laden with fat, there was no glial response. The blood vessel system was not affected.

In agreement with the preserved cyto-architecture was the condition of the myelo-architecture and of the axis cylinders; myelin sheaths and axis cylinders were distinctly brought out and did not show pathologic phenomena; they were not reduced in numbers (figs. 5, 6, 7 and 8).

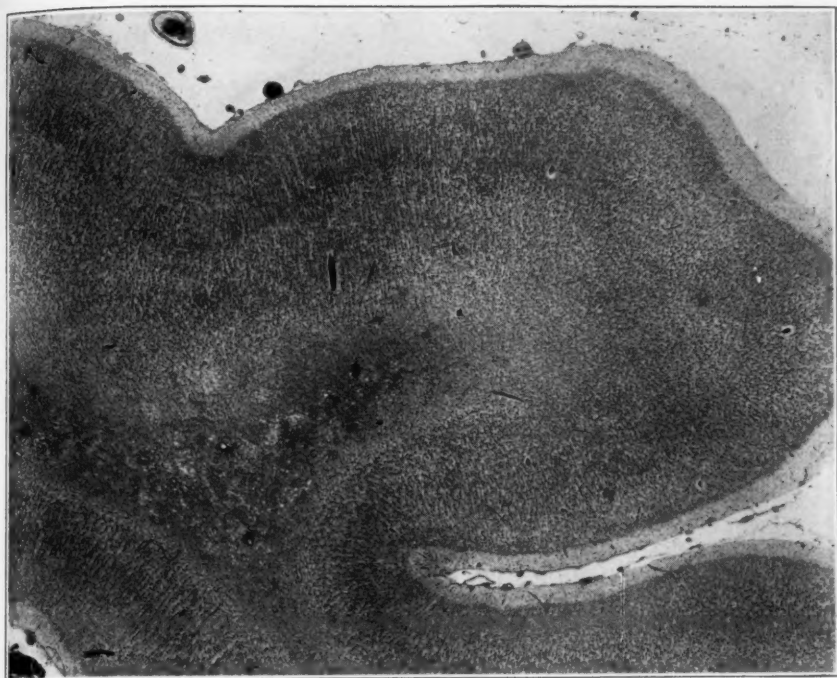


Fig. 4.—The meninges and cortex are normal. The white matter is shrunken and rich in cells. Spongy state. Nissl stain; Zeiss mikroplanar, 35 mm.

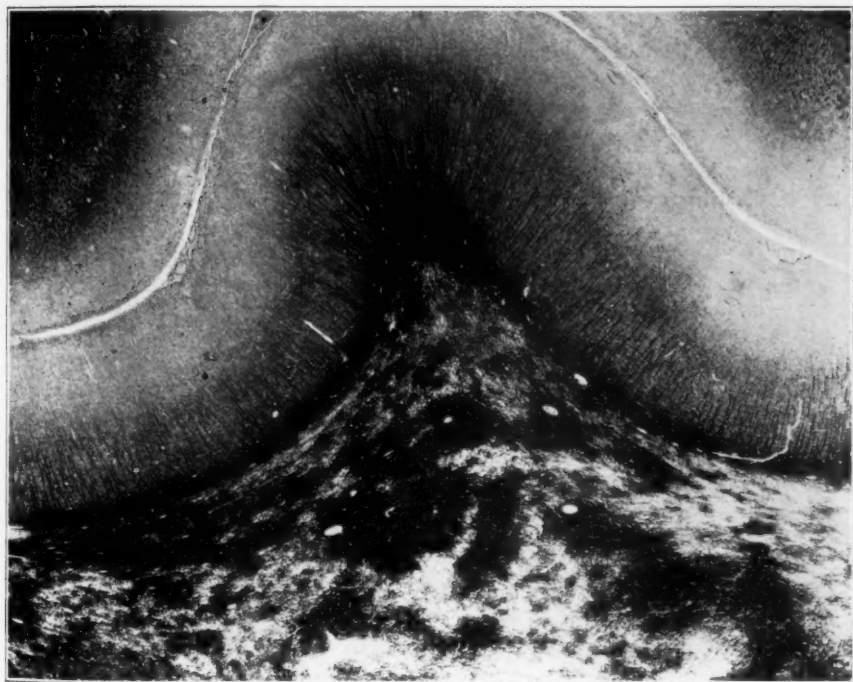


Fig. 5.—The myelo-architecture is normal. The U fibers are well preserved. There are multiple perivascular islands of white matter in the deeper layers. Weigert-Kultschitzky stain; Zeiss mikroplanar, 35 mm.

Microscopic examination of the white matter revealed frequently the perivascular character of the myelin islands, which were connected one with another by a fine myelin network (fig. 7). Under a higher power lens, the myelin sheaths showed definite pathologic changes, such as swelling, thinning, fragmentation and tortuosity, especially at the periphery of the islands (fig. 7).

In Bielschowsky sections the axis cylinders were as numerous as the myelin sheaths, so that axis cylinder islands could be seen in silver preparations as distinctly as myelin islands in Weigert sections. The axis cylinders were tortuous and fragmented between the islands and in their periphery (fig. 8).

Fat preparations showed only occasional small accumulations of lipoids in blood vessel walls or a few gitter cells laden with fat in the rarefied tissue structure. The preserved myelin was stained diffusely yellowish brown with sudan III, so

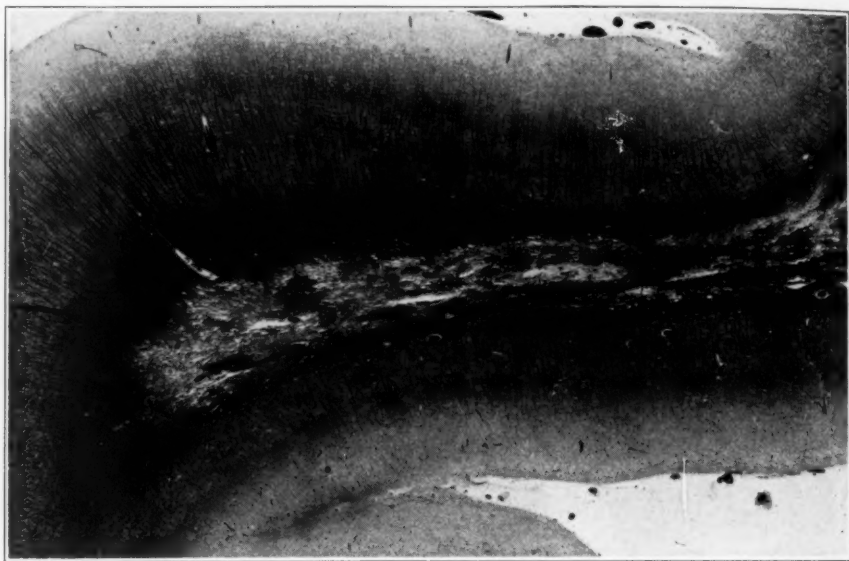


Fig. 6.—A convolution with almost entirely destroyed white matter. The U fibers are well preserved. There are numerous myelin islands. Weigert-Kultschitzky stain; Zeiss mikroplanar, 35 mm.

that the myelin islands appeared almost as distinctly as in Weigert sections. Nissl sections failed to reveal inflammatory changes. The white matter appeared to be rich in nuclei and also frequently spongy in appearance, but this was a pseudo-increase in cells brought about by the shrinkage of the tissue (fig. 4).

There was no glial activity in the white matter except for a few small giant cells. A consolidation of the destroyed tissue had not taken place.

The parenchyma of the caudate nucleus, putamen and pallidum was not affected. There was no glial response, and there was no irritation of the blood vessel system. Somewhat different were the histologic findings in the thalamus, the red nuclei and the central gray and black substances. Here there were numerous glial elements laden with greenish pigment, and a part of the parenchymal cells was reduced to shadows; in the substantia nigra only the red zone was affected. In Weigert sections there was a diffuse demyelination in the pallidum and thalamus, without island formation.

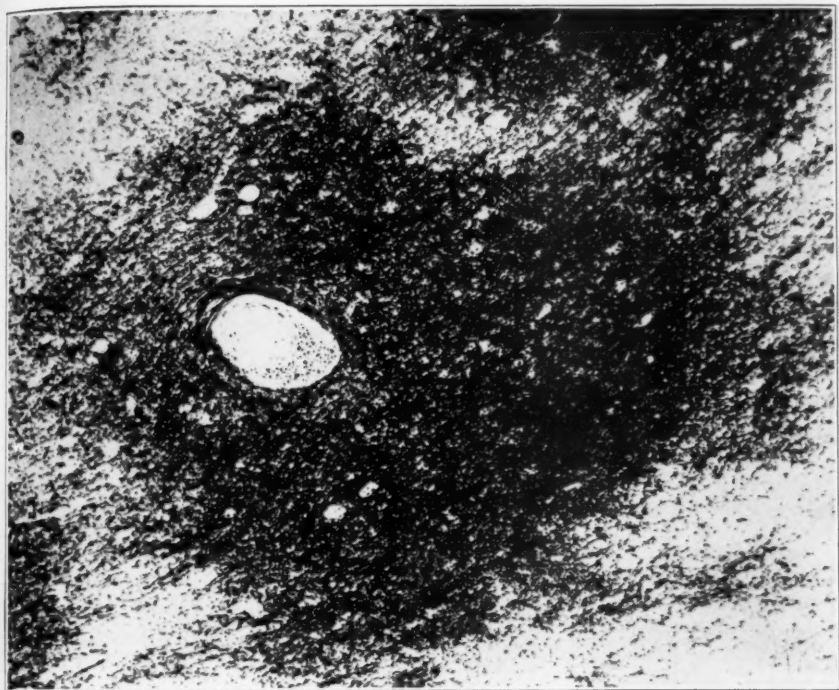


Fig. 7.—A perivascular, considerably rarefied myelin island. Weigert-Kultschitzky stain; Zeiss mikroplanar, 20 mm. OK. I.

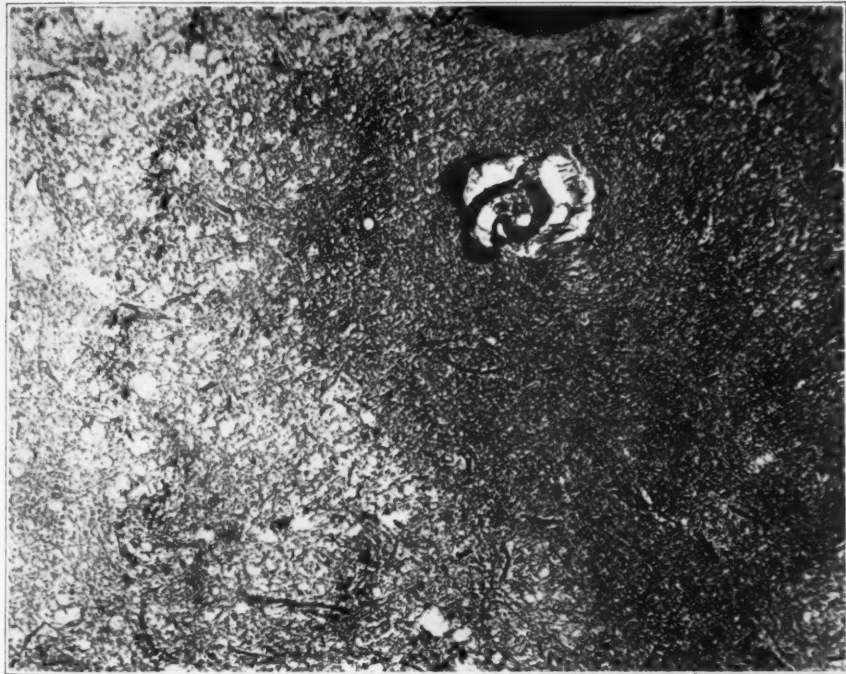


Fig. 8.—A perivascular axis cylinder island; in the left side of the picture fine rarefied axis cylinders are seen. Bielschowsky section; Zeiss mikroplanar, 20 mm. OK. I.

The subthalamic body, the pons, the medulla and the spinal cord were unchanged. The optic nerves were normal.

In Nissl sections, the white matter of the cerebellum appeared richer in nuclei than normal, but Weigert sections disclosed only a slight diffuse demyelination without the formation of islands.

*Summary.*—The anatomic and histopathologic picture was characterized by an advanced atrophy of the white matter of both hemispheres, with preservation of perivascular myelin islands, without severe deformation of the brain outlines and with but slight involvement of the cortex. The cyto-architecture as well as the myelo-architecture of the latter was slightly affected in a few places. The basal ganglia showed a slight diffuse demyelination in the pallidum and thalamus, and a glial response and unspecific changes of the parenchyma in the thalamus, substantia nigra, red nuclei and central gray substance. There was but slight demyelination in the cerebellum. The disease is, therefore, mainly a degenerative one of the white matter of the hemispheres.

#### CLINICAL COMMENT

Clinically, this case presents many differences from the cases described by Pelizaeus and Merzbacher,<sup>1</sup> Bodechtel<sup>4</sup> and Bielschowsky and Henneberg.<sup>3</sup>

In the observations of Pelizaeus and Merzbacher,<sup>1</sup> the disease appeared in four generations of the same stock. Of the fourteen persons afflicted, only two were female. The mode of transmission was, chiefly, through unaffected females to males. In three cases nystagmus was observed at birth. In the majority of patients symptoms developed by the age of 3 months, and in only one as late as 12 months. From the onset of symptoms until the sixth year, progression was rapid; after that it became slower. Spasticity, particularly of the lower extremities, appeared early in the course. Ataxia, predominating in the arms, intention tremors, dysarthria and paresis of the muscles of the back, abdomen, hips and legs, pronounced contractures, muscular atrophies, athetoid and choreiform movements, vasomotor disturbances (cyanosis), trophic changes, skeletal deformities, masklike facial expression and bradylalia were among other findings observed in certain of the cases. Exaggeration of deep tendon reflexes, especially of the lower extremities, with other associated reflexes, such as a positive Babinski sign, as well as loss of umbilical reflexes, was the general rule. Atrophy of the optic nerve was an uncommon finding. Sensory changes and sphincter disturbances were not observed. Some patients showed preservation of normal mentality. In others, with the progression of the process, mental enfeeblement developed. Advanced paresis and atrophies, athetosis and vasomotor and trophic disturbances were frequent. The chronicity of the disease is evident from the fact that the majority of patients lived beyond the age of 20, and that one died at 52. In the cases of Bielschowsky and Henneberg<sup>3</sup> and of Bodechtel,<sup>4</sup> the primary difference was in the

age of onset, which was in the juvenile period; our observations failed to disclose satisfactory evidence of hereditary factors.

A short summary of the clinical symptoms proves that it is not admissible to regard the disease reported by Pelizaeus and Merzbacher<sup>1</sup> and by Spielmeyer and Liebers<sup>2</sup> and the one described here as identical. The difference lies in the outspoken heredity in the observation of Pelizaeus and Merzbacher,<sup>1</sup> with the onset in infancy, whereas we are dealing with a chronic disease of the brain, apparently not hereditary, and with the onset in the fifth decade of life.

The presence of a number of symptoms common to both diseases, as spasticity, ataxia, tremor, dysarthria and reflex anomalies, does not allow them to be considered as related, as these symptoms may appear in different diffuse diseases of the brain.

#### COMMENT ON PATHOLOGY

Patho-anatomically, we group our case with two heredofamilial cases described by Merzbacher<sup>1</sup> and Spielmeyer and Liebers,<sup>2</sup> and two sporadic ones described by Bielschowsky and Henneberg<sup>3</sup> and Bodechtel.<sup>4</sup> We derive from the description given by Merzbacher<sup>1</sup> the following main points: The brain was diminished in size; the convolutions were atrophic, the atrophy being brought about by an advanced destruction of the white matter; the gray matter of the brain appeared to be normal.

Weigert sections disclosed pictures that are highly characteristic of this type of demyelination: The white substance of the hemispheres was atrophic, but there remained numerous islands of myelin communicating one with another; the destruction was particularly advanced in the frontal, temporal and occipital lobes, as well as in the cerebellum; the U fibers were for the most part preserved; there was a slight glial production in the thalamus, but otherwise scarcely any tissue activity.

The findings of Spielmeyer and Liebers<sup>2</sup> were practically the same, but there was a considerable glia fiber production in the white matter.

The pons, the spinal cord and, particularly, the cerebellum were involved in the disease.

By the courtesy of Prof. W. Spielmeyer of Munich, we are in position to compare his findings with ours, as can be seen in figure 9, which represents the second case from the family described by Pelizaeus and Merzbacher.<sup>1</sup> As the picture shows, the patho-anatomic characteristics are fundamentally the same as in our case, but the myelo-architecture is far more affected and the myelin islands are less numerous.

The findings of Bielschowsky and Henneberg<sup>3</sup> and Bodechtel<sup>4</sup> are essentially uniform. The brain was described as atrophic, but without particular change of its configuration by Merzbacher,<sup>1</sup> Spielmeyer and Liebers<sup>2</sup> and ourselves. Bielschowsky and Henneberg,<sup>3</sup> on the contrary, noticed no such atrophy of the convolutions.

The cerebellum was found distinctly diminished in size by Merzbacher, but seemed to be normal in all other cases, including our own. The basal ganglia were reported grossly unchanged in all cases. The pons and medulla were diminished in size in Merzbacher's<sup>1</sup> case, but seemed otherwise unchanged. Spielmeyer and Liebers<sup>2</sup> noted a distinct

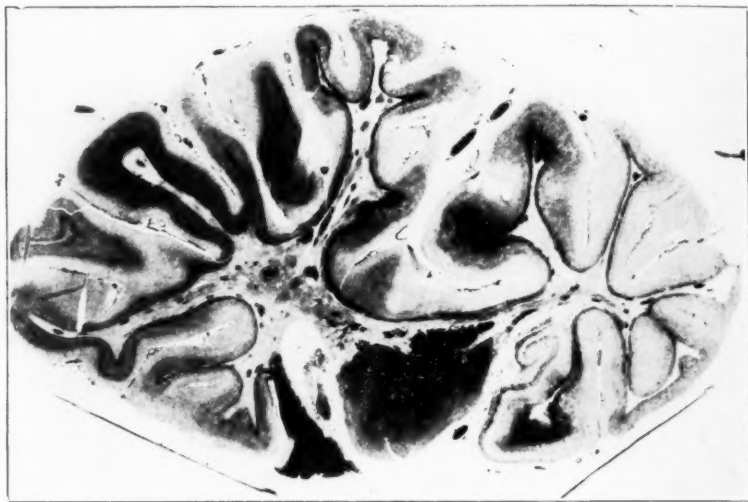


Fig. 9.—Second case of Pelizaeus-Merzbacher's disease (observation by Spielmeyer, Munich). Numerous myelin islands and U fibers are well preserved. The myelo-architecture is considerably degenerated. Weigert section. (Photograph courtesy of Prof. W. Spielmeyer, Munich.)

demyelination; Bielschowsky and Henneberg<sup>3</sup> and we found both formations grossly normal.

The atrophy of the convolutions was uniformly brought about by atrophy of the white matter, which in all cases contained numerous white myelin islands varying in size and irregularly distributed. The destroyed myelin in our case was a smoke gray, although in places it was somewhat bluish in appearance. This is in agreement with Spielmeyer and Liebers.<sup>2</sup>

In three cases the U fibers were comparatively well preserved (Merzbacher,<sup>1</sup> Bielschowsky and Henneberg<sup>3</sup> and our own), whereas,

Spielmeyer and Liebers<sup>2</sup> and especially Bodechtel<sup>4</sup> reported much more advanced destruction. The cyto-architecture of the gray matter was normal in all cases. The myelo-architecture did not show any changes in Merzbacher's<sup>1</sup> case and very slight ones in ours, but the destruction was considerable in the observations of Spielmeyer and Liebers<sup>2</sup> and especially those of Bodechtel.<sup>4</sup>

Spielmeyer and Liebers,<sup>2</sup> Merzbacher<sup>1</sup> and Bielschowsky and Henneberg<sup>3</sup> found a far advanced destruction of the myelin in the cerebellum. Bodechtel,<sup>4</sup> on the other hand, reported only slight changes, and the same was noticed by us.

The corpus callosum was affected in all instances. The spinal cord was intact in our case, but the cervical cord was reported as atrophic by Spielmeyer and Liebers.<sup>2</sup>

The degenerative character of the disease was identical in all cases. The myelin islands were frequently perivascular.

In Merzbacher's<sup>1</sup> case and in our case, the islands were connected with one another by a rarefied myelin network. The well known thinning and swellings of degenerating myelin sheaths and axis cylinders were present in all cases.

The glial response has been variable. Merzbacher reported a slight increase in glia fibers in the optic thalamus only, which is similar to our case, whereas Spielmeyer and Liebers<sup>2</sup> and Bodechtel<sup>4</sup> found a polymorphic, and Bielschowsky and Henneberg<sup>3</sup> an isomorphic gliosis.

The fat metabolism also shows slight variations; in our case there was a negligible amount of it in gitter cells and the perivascular spaces; Bielschowsky and Henneberg<sup>3</sup> reported considerable amounts of fat, and Bodechtel<sup>4</sup> and Spielmeyer and Liebers<sup>2</sup> moderate amounts.

The cerebellum showed the greatest deviations histologically. It was almost entirely destroyed in the cases of Merzbacher,<sup>1</sup> Spielmeyer and Liebers<sup>2</sup> and Bielschowsky and Henneberg,<sup>3</sup> less so in Bodechtel's<sup>4</sup> case, and only slightly in ours.

The medulla and pons were demyelinated in the cases observed by Spielmeyer and Liebers,<sup>2</sup> and much less so in the other three cases, while there were no changes in ours.

The myelo-architecture was histologically intact in the cases observed by Merzbacher, and practically intact in ours. Spielmeyer and Liebers<sup>2</sup> and Bielschowsky and Henneberg,<sup>3</sup> however, reported considerable involvement.

The blood vessel system was involved in no instance.

In the accompanying table we present a summarized comparison of all cases reported to date.

Exhaustive comparison of all cases in question justifies the assumption that we are dealing with an identical patho-anatomic condition. The conformity is so far-reaching that in the face of this the deviations

mentioned can be considered negligible. We call attention to the fact that there were slight deviations from one another in the cases of Merzbacher and of Spielmeyer and Liebers, which occurred in the same family, so that we think that the opinion given has sufficient basis.

*Summary of Cases Reported to Date*

Authors	No. of Cases	Clinical Findings				Patho-Anatomy	Histopathology
		Age of Onset	Heredit-ity	Dura-tion	Chief Symptoms		
Pelizaens and Merzbacher	14	At birth or within 3 mos.	Posi-tive	20 yrs. or more	Nystagmus; spasticity; ataxia; trophic disorders; mental deterioration	Atrophy of brain and cerebellum (1 case)	Gray matter normal; U fibers and interconnected myelin islands preserved; degenerative character; no glial response; little fat (1 case)
Spielmeyer and Liebers	1	.....	.....	.....	.....	Atrophy of brain	Myelo-architec-ture considerably affected; U fibers and interconnected myelin islands preserved; degenerative character, polymorph glial response; moderate amounts of fat
Bielschowsky and Henneberg	1	Juvenile (?)	?	A few years	Feebleminded; otherwise, little known	No atrophy of brain, but advanced atrophy of cerebellum	Myelin islands preserved; degenerative character, isomorph glial response; considerable amounts of fat
Bodechtel	1	5th year	?	12 yrs.	Feebleminded; intention tremor; convulsions; spasticity of lower extremities; ataxia; disturbance of gait; choreiform movements	Brain small; moderate atrophy of cerebellum	Myelo-architec-ture severely affected, myelin islands preserved; degenerative character, polymorph glial response; considerable amount of fat
Löwenberg and Hill	1	5th decade	None	11 yrs.	Stiff gait; tremor and ataxia; generalized hyperreflexia; Babinski sign on right; progressive intellectual deterioration; paranoid trends; dizziness	Atrophy of brain; slight atrophy of cerebellum	Myelo-architec-ture slightly affected; U fibers preserved; myelin islands numerous; degenerative character, no glial response; almost no fat; cyto-architecture normal

This condition must be considered as a process which advances slowly, and there is no reason to believe that the glial aplasia is responsible for it. We are entirely in agreement with the views of Spielmeyer, in spite of the fact that there was no glial proliferation in our case; the advanced age of our patient makes an assumption of aplasia unwarranted.

For the classification of these diseases, the type of destruction of the white matter and the degenerative character of the lesions are deciding

factors. We have to consider our case as belonging to one of the groups of diffuse sclerosis. The decision as to which group is difficult, because all schemes offered are primitive. The older classification distinguished three types: (1) inflammatory, (2) degenerative and (3) blastomatous or dysplastic. This classification disregards the clinical side of the problem, and Bielschowsky and Henneberg advanced, therefore, a different conception. These authors distinguished a hereditary group of diffuse sclerosis, which they called leukodystrophia cerebri progressiva hereditaria and which is subdivided into three divisions: (1) infantile, (2) juvenile and (3) chronic, the cases described by Pelizaeus and Merzbacher and Spielmeyer and Liebers belonging to the last subdivision.

The attempt to utilize one of the classifications mentioned for our case meets with great difficulties. If the term degenerative diffuse sclerosis is selected, one is compelled to classify the case in question with a number of observations of entirely different histologic character, which are regarded as degenerative merely because of lack of inflammatory phenomena.

If the classification of Bielschowsky and Henneberg is used, the clinical deviations cannot be reconciled, as has already been pointed out.

Hypothetically, it seems reasonable to subdivide cases with demyelination of the type here described into two groups: (1) hereditary and (2) sporadic; to the latter belong the observations of Bodechtel, Bielschowsky and Henneberg and ourselves. But such an assumption must be based on additional observations.

It is obvious that the classifications so far advanced are based on few clinically different observations, so that no definite conclusions can be reached. A definite classification can be based only on a knowledge of etiology, as yet undetermined.

#### CONCLUSIONS

1. Diseases of the brain which are patho-anatomically identical with those reported by Pelizaeus and Merzbacher and Spielmeyer and Liebers have been observed sporadically.
2. These conditions are not identical clinically with those reported by Pelizaeus and Merzbacher and may appear in childhood as well as later in life.
3. The syndrome described is a diffuse chronic degenerative disease of the white matter and not an aplasia of the myelin.
4. The disease described must be regarded at the present as a subdivision of diffuse sclerosis.

## LYMPHOBLASTOMATOUS INVOLVEMENT OF THE NERVOUS SYSTEM

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The seven reports given in this paper serve to illustrate the various clinical manifestations of lymphoblastomatous involvement of the nervous system. In three of the cases the lesions were predominantly cerebral; in one, cerebellar and in another, meningeal; in the other two, the cranial nerves and the spinal cord were most disturbed. The cases, therefore, will be classified under these gross headings as a matter of convenience. Practically all of the so-called "cerebral cases," however, showed evidence of involvement of the cranial nerves at one time or another, and at least one showed evidence of cerebellar disease.

The term "lymphoblastoma" requires a word of explanation. It was suggested by Mallory to describe those tumors the cell type of which is the lymphoblast, the precursor of the adult lymphocyte. Owing to the confusion of terminology in the literature, in which one finds lymphogranuloma, lymphosarcoma, Hodgkin's lymphogranuloma and pseudoleukemia used indiscriminately, the impression is gained that each of these represents a well defined clinical entity. When to these are added chronic lymphatic leukemia in its aleukemic form and the cutaneous manifestations of lymphoblastoma under still another name, mycosis fungoides, the confusion becomes overwhelming indeed. For this reason there has been a tendency in recent years to group all these diseases under the generic term, lymphoblastoma, adding a qualifying clinical classification. Thus, lymphatic leukemia becomes lymphoblastoma leukemicum; aleukemic lymphatic leukemia, lymphoblastoma aleukemicum; mycosis fungoides, lymphoblastoma cutis; Hodgkin's disease, lymphoblastoma (Hodgkin's type), and lymphosarcoma, lymphoblastoma (infiltrating type). When it is observed, clinically, that a case of leukemia may become aleukemic or even pseudoleukemic (that is, with no abnormal blood picture) during the course of the disease, and that Hodgkin's disease may show sarcomatoid infiltrations of the skin like those of mycosis fungoides, such a classification, as has been proposed by one of us (Dr. Hunter), permits of a better understanding of this group of

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tumors. The scheme is by no means final; it may be radically changed as we learn more about the multiple varieties of lymphoblastomas.

There is a paucity of literature on all forms of lymphoblastoma, except the Hodgkin's type, as it affects the nervous system. This syndrome has received particular attention by Eugénis,<sup>1</sup> who reviewed, in his University of Lyon thesis, all the reported cases up to 1929. He found fifty-four in which the nervous system had been invaded by Hodgkin's disease, the first case being that of Murchison and Sanderson,<sup>2</sup> described in 1870. Eugénis reported one case not previously described (case 41). In twelve instances the involvement was cranial; in forty-two, spinal. A second recent review of Hodgkin's disease, with a complete bibliography, is that of Chevallier and Bernard.<sup>3</sup> This monograph covers all aspects of the disease, the neurologic manifestations being incidental to the whole. In addition to the many references given by these authors, scattered reports by Favre,<sup>4</sup> Hare and Lepper,<sup>5</sup> Howell and Gough,<sup>6</sup> Johnston,<sup>7</sup> Konowalow and Chondkarian,<sup>8</sup> Poynton and Harris,<sup>9</sup> Reese and Middleton,<sup>10</sup> Shapiro,<sup>11</sup> and Weil<sup>12</sup> point to an unusual interest in the nervous aspects of this disease.

1. Eugénis, Cimon: Les manifestations cérébro-médullaires de l'adénie éosinophilique prurigène, Thèse de Lyon, 1929.

2. Murchison, C., and Sanderson, J. B.: Case of "Lymphadenoma" of the Lymphatic System, Spleen, Liver, Lungs, Heart, Diaphragm, Dura Mater, etc., Tr. Path. Soc. London **21**:372, 1870.

3. Chevallier, P., and Bernard, J.: La maladie de Hodgkin; lymphogranulomateuse maligne, Paris, Masson & Cie, 1932.

4. Favre, M.; Dechaume, J., and Croizat, P.: J. de méd. de Lyon **12**:757 (Dec. 20) 1931.

5. Hare, D. C., and Lepper, E. H.: Two Cases of Lymphogranulomatosis Maligna, One with Involvement of the Vertebral Periosteum, Lancet **1**:334 (Feb. 13) 1932.

6. Howell, A., and Gough, J.: Acute Lymphatic Leukaemia with Facial Diplegia and Double Abducens Palsy, Lancet **1**:723 (April 2) 1932.

7. Johnston, J. M.: Hodgkin's Disease with Invasion of Spinal Column; Pressure on Cauda Equina; and Degeneration of Posterior Columns of the Cord, Pennsylvania M. J. **34**:877 (Sept.) 1931.

8. Konowalow, N. W., and Chondkarian, O. A.: Zur Klinik und pathologischen Anatomie der Rückenmarkläsionen bei Lymphogranulomatose, Arch. f. Psychiat. **95**:350, 1931.

9. Poynton, F. J., and Harris, K. E.: A Case of Paraplegia in Hodgkin's Disease, Lancet **2**:903 (Oct. 25) 1930.

10. Reese, H. H., and Middleton, W. S.: Mechanical Compression of the Spinal Cord by Tumorous Leukemic Infiltration, J. A. M. A. **98**:212 (Jan. 16) 1932.

11. Shapiro, P. F.: Changes of the Spinal Cord in Hodgkin's Disease, Arch. Neurol. & Psychiat. **24**:509 (Sept.) 1930.

12. Weil, Arthur: Spinal Cord Changes in Lymphogranulomatosis, Arch. Neurol. & Psychiat. **26**:1009 (Nov.) 1931.

The actual type of lymphoblastoma is not always clearly indicated in the cases reported; Hodgkin's disease is by far the most common. Reese and Middleton,<sup>10</sup> however, reported one case of lymphoblastoma leukemicum (acute lymphatic leukemia), another, probably lymphoblastoma aleukemicum and a third, lymphoblastoma cutis. In the first case, that of paraplegia with a block in the spinal fluid, there was found at necropsy an epidural tumor of the spinal cord composed of lymphoid tissue. In the second case, that of spastic paraplegia with partial block, an operation was performed and an extradural tumor found. There was a good response to subsequent roentgen treatment; two years later the patient died; there was no necropsy. The patient was always aleukemic. The third case reported by Reese and Middleton is one of lymphoblastoma cutis, with associated peripheral nerve paralysis. The roentgen response was fairly good, but it is not definitely stated whether or not the peripheral nerves recovered. Howell and Gough,<sup>6</sup> also, reported a case of lymphoblastoma leukemicum with facial diplegia and bilateral abducens palsy. At necropsy lesions were found in the right frontal lobe and pons.

The following seven cases serve to emphasize the point already noted from a study of the literature and add a number of details not hitherto brought forward:

#### REPORT OF CASES

*CASE 1.—Lymphoblastoma, infiltrating type. Anemia, with otherwise normal blood. Cerebral involvement six months after the original diagnosis. Neurologic symptoms and signs variously affected by roentgen therapy. Death, nine months after onset. Biopsy. Necropsy.*

*History.*—I. E., an American housewife, aged 54, referred by Dr. Richard G. Wadsworth, was first seen on Dec. 27, 1929, complaining of fulness on the nasal side of the right eye. Sixteen years previously a "lipoma" had been removed from the subcutaneous tissue over the left scapula. About September, 1929, the patient noticed a recurrence of swelling in the same area. Early in December, the scapular tumor and a subcutaneous tumor under the right clavicle, 3 by 1 cm., were removed.

Pathologic examination of the biopsied tissue showed rapidly growing lymphoblastoma (lymphosarcoma).

*Examination.*—The right eye showed slight exophthalmos, and at the inner canthus there was a small, soft swelling, but no definite mass was felt. Deep in the left side of the pelvis, a firm, movable mass, 3 by 2 cm., was palpated.

Examination of the blood showed 3,500,000 red corpuscles per cubic millimeter.

*Treatment and Course.*—The patient received a series of high voltage roentgen treatments to the right orbit; three days later, the exophthalmos had disappeared.

On March 10, 1930, the patient complained of difficulty in speech of a few days' duration. A nodule, 1 cm. in size, was found in the skin just above the left elbow. Three days later the patient had three attacks of jacksonian epilepsy, involving the right side of the face and lasting a minute or two. Examination at this time showed slight apathy; the patient laughed easily; there was difficulty in speech, but she made mistakes in choosing words rather than in pronunciation; there was haziness of the fundus of the left eye, weakness of the right grip, and thumb-to-finger-tip counting was awkward on the same side. The patient was again given

high voltage radiation to the left side of the skull. Four days later there was practically no impairment of speech. The right facial weakness, which had developed a few days prior to this time, disappeared, as well as the awkwardness in counting fingers. Two small hemorrhages were present at the lower border of the left optic disk.

On March 29, 1930, a left homonymous hemianopia was demonstrated. Again roentgen therapy to the right side of the skull was instituted, and a week later



Fig 1 (case 1).—Tumor infiltrating the cerebrum and breaking through the pia mater to extend along the subarachnoid space.

there was considerable lessening of the hemianopia and a moderate amount of improvement in the mentality.

On April 21, 1930, astereognosis of the right hand and some weakness of the right grip were again noted. There was difficulty in walking, of the cerebellar, ataxic type, with a tendency to fall to the left.

On April 26, 1930, lumbar puncture revealed: initial pressure of 300; rise on combined jugular compression to 450; after withdrawal of 5 cc., 210; after withdrawal of 10 cc., 160; cells, 11 lymphocytes per cubic millimeter; total protein, 93 mg.

per hundred cubic centimeters; colloidal gold curve, 0001123210; Wassermann test, negative.

During May and June, 1930, the patient showed a general tendency toward a progressive downward course. There was considerable variation from day to day in the neurologic findings. At one time she was deeply comatose; she improved on the following day. The optic disks showed choking, which cleared up for a time, only to recur. Bradycardia was observed, which was generally coincident

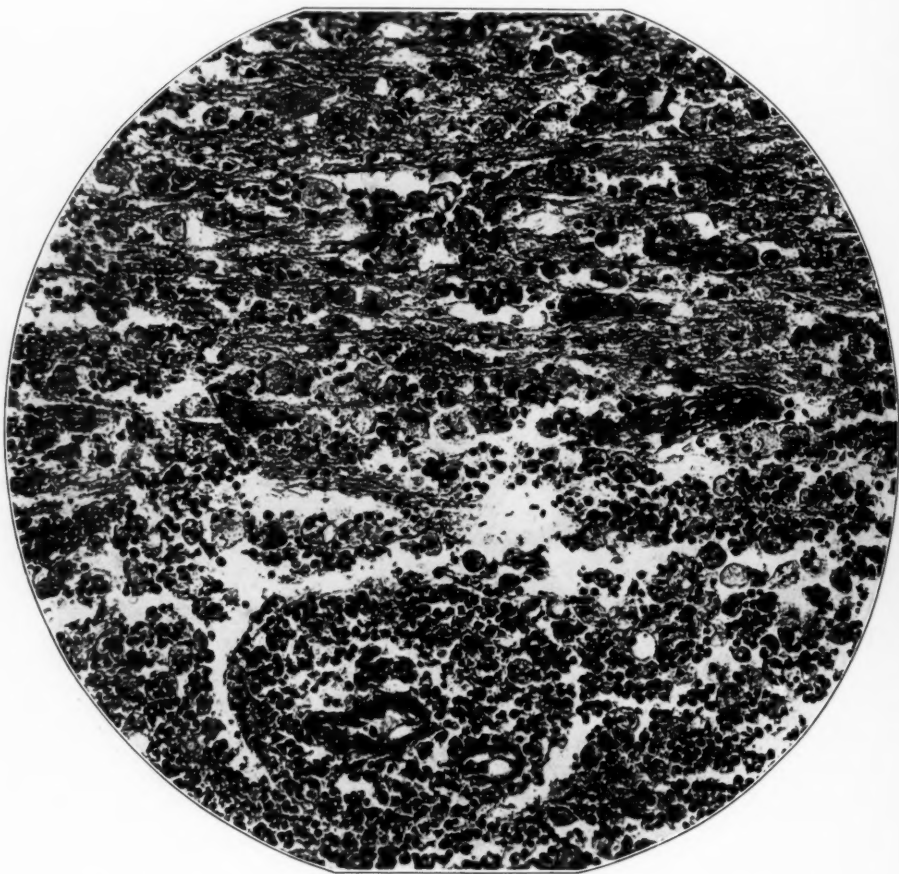


Fig. 2 (case 1).—Microscopic appearance of the infiltrating tumor of the cerebrum.

with increased choking of the optic disks. A tumor appeared in the left parotid region and regressed spontaneously. The patient's mental condition became progressively worse. She died on June 16, 1930.

*Necropsy* (Dr. Tracy B. Mallory).—Tumors in the suprarenal gland, ovary, brain, orbital and pituitary regions showed essentially similar microscopic pictures. At the periphery of the various tumors, where there was active invasion of the surrounding tissues, tumor cells were numerous. They were round, and showed clear vesicular nuclei with large nucleoli; the cytoplasm was rather scant,

nongranular and strongly basophilic. The cells lay irregularly in the meshes of a delicate, scarcely visible reticulum, without orderly arrangement. This appearance was indistinguishable from that of lymphoblasts. Mitotic figures were present in moderate numbers. The central portions of all the tumors presented a most unusual appearance. Tumor cells were relatively infrequent and most of the mass was made up of extremely large phagocytic cells, containing from two to ten pyknotic spherules, probably the degenerating nuclei of ingested tumor cells. A

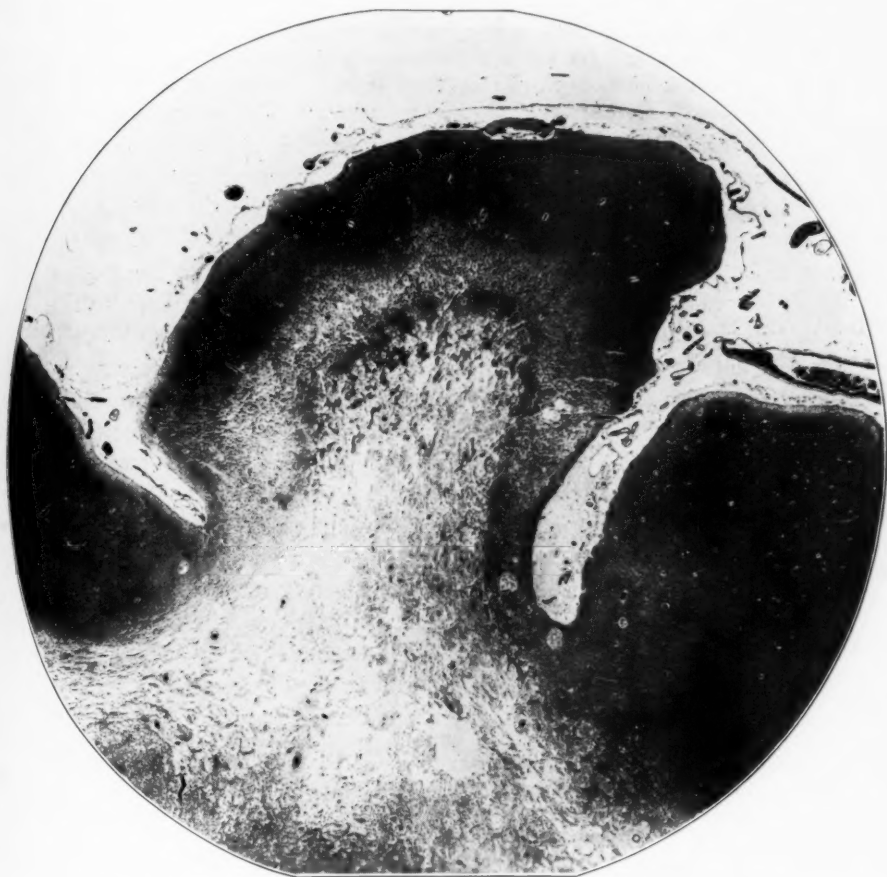


Fig. 3 (case 1).—Detail of lesion in left anterior central convolution.

review of the original biopsy made at another hospital showed similar phagocytes among the tumor cells. Sections of two of the largest lymph nodes showed active myelopoiesis and hematopoiesis, but no evidence of lymphoma. In spite of the most extraordinary distribution of the tumor masses, the character of the tumor cells seemed certain enough to warrant a diagnosis of lymphosarcoma.

Microscopic Examination of the Brain (Dr. Charles S. Kubik): The lesion in the right hemisphere was similar in all respects to the tumors of the suprarenal gland, ovary and right orbit. It infiltrated the surrounding tissues (figs. 1 and 2), extended along the perivascular spaces, and at one point broke through the pia

and extended for a short distance along the subarachnoid space. In a nearby fissure the subarachnoid space was free from cells. The lesion of the left anterior central convolution consisted of a focus of degeneration, involving chiefly the white matter but also the deeper layers of the cortex, and in one place extending practically through to the pia. The margins of the lesion were not sharply defined (fig. 3). In the central degenerated portion and also in the surrounding tissues there were numerous gitter cells. Gitter cells were also thickly packed in the perivascular spaces and extended out into the subarachnoid space. A few scattered cells having the appearance of lymphocytes were noted in several perivascular spaces, but there was nothing that resembled the tumors of the right cerebral hemisphere, orbit, suprarenal gland and ovary. There was a proliferation of glial elements in the immediate vicinity of the degenerated area. The subarachnoid space, with the exceptions noted, contained no cellular exudate or infiltration.

*Comment.*—This case ran the usual course of lymphoblastoma of the infiltrating type. There were no changes in the character of the white blood cells, but biopsy and necropsy confirmed the diagnosis. The patient responded well to roentgen therapy. Invasion of the nervous system by the lymphoblastoma occurred six months after the original diagnosis was made. By correlating the pathologic findings with those observed clinically, we can account for all the symptoms. The lesion in the left anterior central convolution led to the jacksonian epilepsy and the attacks of aphasia. This area, thoroughly treated by high voltage roentgen rays, was free from tumor tissue when examined after death, although evidence of pressure or impaired circulation was seen in the degeneration of the cerebral cortex and the deeper layers. The lesion in the right occipital region, moreover, was sufficient to account for the homonymous hemianopia and the general increased intracranial pressure. It had not responded so well to roentgen treatment, as there was still marked evidence of active tumor at this point. The response had been sufficient, however, to reduce the intracranial pressure and, probably, to prolong the patient's life. Certainly as the result of this treatment the symptomatic relief was considerable.

*CASE 2.—Lymphoblastoma, infiltrating type. Tumor of the forehead, of two years' duration, with signs of intracranial involvement. Response to roentgen therapy. Death two and one-half years after original symptoms. Biopsy. No necropsy.*

*History.*—B. Mc., an Irish housewife, aged 49, entered the Massachusetts General Hospital on Dec. 14, 1927, complaining of swelling of the forehead and inconstant headache. In 1925, the patient first noted the tumor, which increased in size for six months and then remained stationary. One month prior to entry, the left eye began to swell, but she complained only of slight blurring of vision.

*Examination.*—There were: a slightly lobulated, rounded, hard and painless tumor, about 4 cm. in diameter, over the left orbit and center of the forehead; edema of the tissues around the left eye; choked optic disks of 2 diopters and weakness of the left external rectus muscle. Lumbar puncture revealed clear, yellowish fluid, with an initial pressure of 450 mm.; 3 lymphocytes per cubic milli-

meter; total protein, 160 mg. per hundred cubic centimeters; colloidal gold curve, 1122333211; Wassermann test, negative.

Roentgen examination of the skull and other bones of the body failed to show any evidence of metastases.

Microscopic examination of the biopsy tissue showed lymphoblastoma or an atypical form of melanoma or endothelial myeloma.

*Treatment and Course.*—High voltage roentgen treatment was given to the skull; the tumor receded. On the day of discharge, Jan. 26, 1928, two small hemorrhages were seen in the right fundus. On March 14, 1928, a gland, about 2 cm. in diameter, was found in each supraclavicular triangle. Under roentgen therapy they disappeared. The patient was last seen on March 19, 1928; at that time there was no sign of the original tumor. She died at home on June 26, 1928. Necropsy was not permitted.

*Comment.*—This case also illustrates the infiltrating type of lymphoblastoma as it affects the cerebrum. Although the sequence of events cannot be so clearly visualized as in case 1, presumably the tumor extended into the frontal lobes. The most important finding was the well marked changes in the cerebrospinal fluid, indicating increased intracranial pressure, with a high total protein. The response to roentgen therapy was immediate, and the patient's symptoms, for the time being, were relieved.

*CASE 3.—Lymphoblastoma, Hodgkin's type (?). Glandular swelling for eight years before first examination. Under observation from 1924 to date, with repeated tumors in many parts of the body. Good response to roentgen treatment. Neurologic manifestations first noted in 1931. Biopsy.*

*History.*—G. B., a schoolboy, aged 10, entered the Massachusetts General Hospital on Aug. 20, 1924, with a large tumor on the left side of the neck. For eight years similar small swellings in the neck had been noted, the first of which broke down and drained. The growth on the left side had increased in size during the last year until, on entry to the hospital, it filled the whole contour between the shoulder and ear.

*Examination.*—There was an enormous, irregular mass of glands in the left side of the neck. The tumors were soft and circumscribed; the trachea was displaced to the right. The spleen was palpable, extending downward to the level of the umbilicus and to within 2 inches of the midline. Roentgen examination of the chest gave negative results. A blood count and smear were normal. The patient had fever, up to 101 F., while in the hospital. Biopsy, on Aug. 28, 1924, showed malignant lymphoma, type not specified.

*Treatment and Course.*—During the period from August, 1924, to May, 1931, tumors developed in the mediastinum, spleen, liver and abdomen, accompanied by an extreme anemia, with the appearance of new glands. The tumors responded remarkably well to high voltage roentgen irradiation; whenever this treatment was instituted the enlarged glands disappeared and the anemia cleared up. During the six years he was under observation, he entered the hospital seven times for roentgen therapy; in addition, numerous treatments were given in the clinic for ambulatory patients.

*Subsequent Admission.*—On May 4, 1931, the patient was again admitted to the hospital. His chief complaints were: headache, vomiting, mental sluggishness and difficulty in talking. There was slight fever, which lasted a few days. Examina-

tion revealed mental torpor, aphasia, considerable loss of weight and extreme pallor. Examination of the blood showed: 18,000 white blood corpuscles and 2,080,000 red blood corpuscles per cubic millimeter; hemoglobin, 35 per cent.

An epilating dose of high voltage roentgen irradiation was given to each side of the skull, 650 roentgens to the left side and 400 roentgens to the right.

On June 1, 1931, the patient was greatly improved; the red blood corpuscles numbered 3,460,000 per cubic millimeter; he was alert mentally. There was still a little difficulty in speech. The right side of the face was slightly weak. The knee jerks were active and equal; there was a bilateral Babinski sign. Another course of treatment, consisting of 644 roentgens to the posterior part of the skull, and 600 roentgens to the anterior part of the skull, was given.

On July 13, 1931, the patient was in better health than he had been since 1924; he had gained 13 pounds (5.9 Kg.) since May; there was no evidence of any glandular enlargement. Neurologic examination gave negative results.

When last seen, on Feb. 8, 1932, the patient was pale; there were enlarged glands in the groin. More roentgen treatment was given. At this time neurologic examination showed: the optic fundi were normal; there was slight weakness of the right corner of the mouth; speech was normal; there was no paralysis of the arms or legs; the deep reflexes in the arms were equal and very active; the knee and ankle jerks were equal and active; there was no clonus or Babinski sign; there was no loss of sensation.<sup>13</sup>

*Comment.*—This case is an example of long-standing lymphoblastoma, probably of the Hodgkin's type. The tumor was present for at least sixteen years. For the past eight years the patient has been under our observation, and has had numerous tumors in all parts of the body. Roentgen therapy has been given repeatedly. An intracranial lesion occurred in 1931, causing symptoms of right hemiparesis and aphasia. These, too, responded well to roentgen therapy, and a year later no clinical evidence of these symptoms was observed. Accurate, rapid neurologic diagnosis led to immediate treatment.

*CASE 4.—Lymphoblastoma leukemicum, aleukemicum and pseudoleukemicum. Glandular involvement for eleven years. Seven years after onset, cranial nerve and cerebellar symptoms. Partial relief by roentgen therapy. Marked variation in blood picture. Pathologic spinal fluid.*

*History.*—J. J. G., a Polish laborer, aged 57, married, entered the Massachusetts General Hospital on May 11, 1925, complaining of swelling of the glands in the neck, axillae and groins. Four years previously he had noticed a tumor, about 2 cm. in diameter, near the elbow on the flexor surface of the right forearm; it disappeared during the following year. Three years before entry there was swelling of the glands of the neck. For two years he had noted that the abdomen was getting larger. For the past year he had had some ringing in the ears.

*Examination.*—There were: generalized enlargement of the cervical, axillary, epitrochlear and inguinal glands, which varied from 1 to 3 cm. in size; the liver descended 10 cm. below the costal margin; the spleen was easily palpable; there was some enlargement of the heart to the left. Examination of the blood showed: white blood cells, 99,200 and red blood cells, 4,096,000 per cubic millimeter; hemoglobin, 70 per cent; lymphocytes, 95 per cent; basal metabolic rate, +30.

13. The patient died at home on March 6, 1933; necropsy was not performed.

*Treatment and Course.*—Roentgen therapy was applied to the spleen, chest, neck, axillae and groins during the next two months.

During 1927, the patient remained in fairly good condition, but in May, 1928, he complained of stiffness and a burning sensation in the left side of the face. Examination showed some anesthesia of the left fifth nerve area and absence of the left corneal reflex.

On June 2, 1928, he complained of attacks of aching in the forehead of seven months' duration; a constant burning sensation in the left side of the face, in the lips and in the left side of the tongue and vertigo and diplopia. He had also noticed unsteadiness in walking, especially in the dark. Neurologic examination at this time revealed slow, irregular lateral nystagmus, with diplopia on looking toward the left; drooping of both eyelids; diminished left corneal reflex; decreased sensation to wool on the left cheek, and decreased hearing on the left (due to old chronic disease of the middle ear?); slight intention tremor of the right hand and some difficulty in walking. The optic fundi showed hyperemia and haziness of the disks, with the small vessels dilated and tortuous; hemorrhages were seen. The visual fields were normal. Examinations of the blood showed: white blood cells, 6,000 per cubic millimeter; lymphocytes, 35 per cent.

Lumbar puncture on June 7, 1928, showed: xanthochromic fluid; initial pressure, 265 mm.; under combined jugular compression, 540 mm.; after withdrawing 5 cc., 150 mm.; after withdrawing 10 cc., 105 mm.; cells, 1 lymphocyte per cubic millimeter; total protein, 336 mg. per hundred cubic centimeters; colloidal gold curve, 1111221100; Wassermann test, negative.

On June 21, 1928, lumbar puncture revealed: slightly xanthochromic fluid; initial pressure, 180 mm.; under jugular compression, 260 mm.; after withdrawal of 5 cc., 85 mm.; after withdrawal of 10 cc., 60 mm.; cells, 3 lymphocytes per cubic millimeter; total protein, 372 mg. per hundred cubic centimeters; colloidal gold curve, 1111221000; Wassermann test, negative.

*Treatment and Course.*—The patient was given high voltage roentgen therapy to the skull, which relieved the facial paresthesia somewhat, but the numbness of the face remained the same.

In April, 1929, the neurologic condition was relatively unchanged. The signs pointed to an extramedullary involvement of the fifth nerve near the gasserian ganglion on the left side; all sensory branches were affected. There was also some weakness of the sixth nerve.

On March 23, 1931, there was difficulty in walking; the patient was free from headache, nausea and blurring of vision. There was marked ataxia, and he walked with the feet wide apart, the left leg being more awkward than the right. The optic fundi showed some arteriosclerosis and possibly slight blurring of the disks. Nystagmus was more marked on looking to the left than to the right. The left fifth nerve was involved, there being paralysis of the motor branch as well as loss of sensation. The knee jerks were active, the right being somewhat more exaggerated than the left. There was no ankle clonus, but on the right side there was a distinct tendency for the big toe to move upward on plantar stimulation. In general, the patient showed signs of a lesion in the cerebellum, as well as destruction of the fifth nerve on the left side. There was no evidence of increased intracranial pressure.

During the summer of 1931, the patient continued in about the same condition and in November no further treatment was advised.

*Comment.*—The patient passed through the leukemic, aleukemic and pseudoleukemic phases of the disease during a period of seven years

under our observation. Neurologic manifestations, chiefly pointing to invasion of the cerebellum and compression of the cranial nerves, occurred seven years after the onset of the disease. The cerebrospinal fluid findings are not dissimilar to those in case 1. Roentgen therapy was only partially successful in clearing up the neurologic manifestations. The lesion in the cerebellum did not respond well and is probably of the deep, infiltrating type noted in the pathologic examination in case 1.

*CASE 5.—Lymphoblastoma leukemicum. Symptoms for one year before death. Acute meningeal involvement. Death. Necropsy.*

*History.*—A. E. G., a man, American, married, a retired stock broker, aged 57, who was referred by Dr. Wyman Richardson, was first seen on Sept. 30, 1930, complaining of acute backache, one year previously and again six months later. About the same time he noted a swelling behind the ear, another in the back of the neck and also one in the groin. He was easily fatigued, and his appetite was poor. Severe occipital and frontal pain was not relieved by medication. He had lost 25 pounds (11.3 Kg.) in weight.

*Examination.*—The patient was acutely ill, with restless movements of the head and arms, groaning and complaining of headache. The optic fundi showed tortuosity of the retinal vessels. Masses of glands in each axilla and a small gland behind the right ear were palpated. The bladder was distended. The right knee jerk was considerably greater than the left. Removal of 12 ounces of clear urine by catheterization immediately relieved the headache; constant drainage of the bladder was employed. The following morning he was better; mentally, he appeared more coherent. The abdomen was soft and the tip of the spleen easily palpable. There were several glands, 3 cm. in diameter, deep in each side of the pelvis. Examination of the blood showed: nonprotein nitrogen, 38 mg. per hundred cubic centimeters; white blood corpuscles, 70,000 per cubic millimeter, all lymphocytes.

*Treatment and Course.*—Roentgen irradiation was not given. On the day of admission the patient became comatose. Examination of the optic fundi showed increasing engorgement of the veins. The right arm was spastic, the knee jerk exaggerated, and the Babinski sign was present on the same side. The patient died the next morning.

Lumbar puncture performed on Oct. 1, 1930, showed that the pressure of the fluid was moderately increased; it could not be accurately read because of the patient's restlessness. The fluid was slightly yellow and cloudy; cells, 750 lymphocytes per cubic millimeter; total protein, 255 mg. per hundred cubic centimeters; colloidal gold curve, 2443333221; Wassermann test, negative.

*Necropsy* (Dr. Shields Warren, Palmer Memorial Hospital).—Glands, 3 by 4 cm. in size, were palpable in the neck, axillae, groins and popliteal spaces. The spleen weighed 410 Gm. The serosal surface of the gastro-intestinal tract showed small white foci, from 1 to 2 mm. in diameter. The lymph nodes were enlarged in the mediastinal, retroperitoneal and pelvic regions, the largest measuring 5 by 3 by 3 cm. The aorta in the lumbar region was displaced from 4 to 5 cm. to the left by the growth of retroperitoneal glands.

Microscopic examination showed small foci of lymphoblasts and lymphocytes in the pleura, peribronchial tissues and alveolar walls throughout the lung. The spleen showed diffuse infiltration of the pulp with lymphocytes and immature

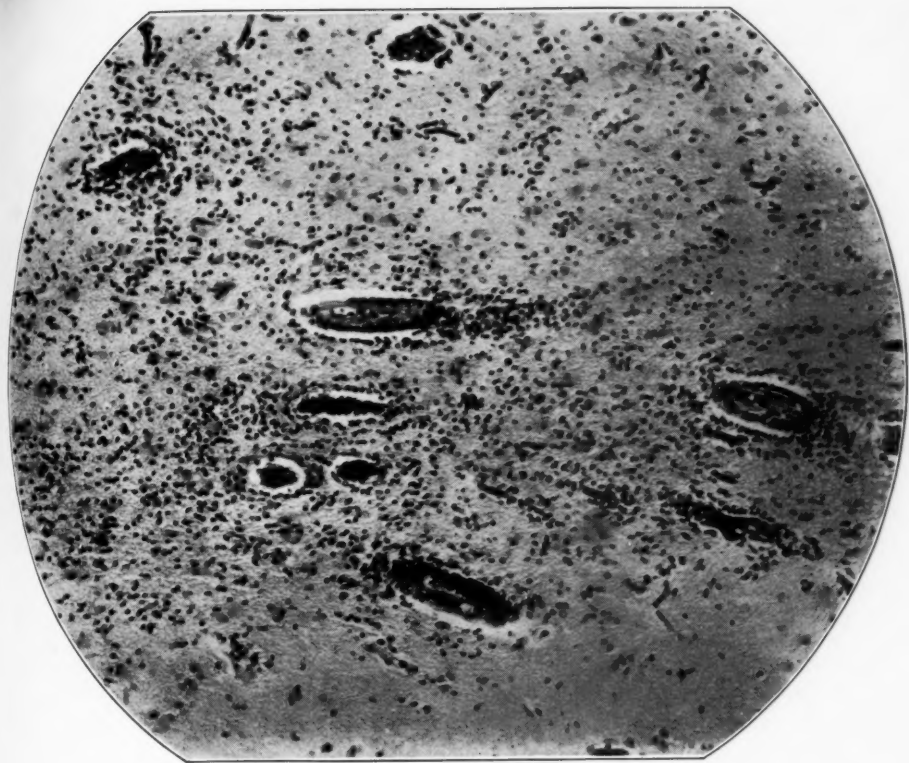


Fig. 4 (case 5).—Lymphoblastomatous infiltration of the cerebrum.

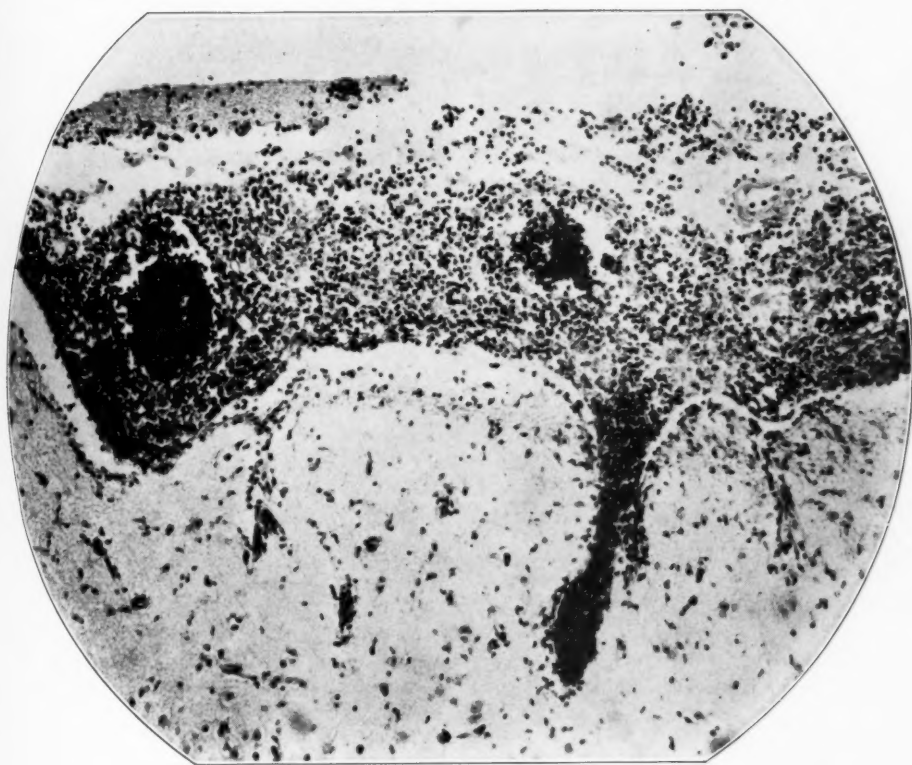


Fig. 5 (case 5).—Lymphoblastoma in the subarachnoid space, "lymphoblastomatous meningitis."

lymphoblasts. Foci of heavy lymphocytic and lymphoblastic infiltration in the submucosa, in some places displacing glands of the mucosa, were noted in the intestines. In the kidney were small foci of immature lymphocytes about some of the vessels and glomeruli. The lymph nodes were almost entirely replaced by large numbers of lymphocytes and lymphoblasts, many of which showed mitotic figures; there were rare tumor giant cells. The cerebrospinal fluid was under slightly increased pressure, but apparently clear. In the left cerebral hemisphere of the brain, on the superior surface in the region of the fissure of Rolando, there were slight swelling and increased firmness. On section, after fixation, a focus of softening was found in the anterior portion of the left internal capsule. The cerebellum was slightly displaced into the foramen magnum. The leptomeninges, over the vertex, were slightly thickened and clouded.

On microscopic examination of the brain, a few small foci of lymphocytic and lymphoblastic infiltration were noted in various parts of the cerebrum, in the region of the larger blood vessels (fig. 4); the perivascular spaces were well filled with tumor tissue; the subarachnoid space contained similar tumor tissue (fig. 5). There were no foci of necrosis or softening.

*Comment.*—The unusual feature of this case was the acute meningeal involvement by lymphoblastoma. So rapid was the onset of the cerebral manifestations that appropriate roentgen treatment could not be given. The cerebrospinal fluid gave evidence of marked meningeal involvement. This was borne out by the necropsy.

*CASE 6.*—*Lymphoblastoma, Hodgkin's type. Glandular involvement of five years' duration. Partially successful roentgen therapy. Cranial nerve palsies four years after onset. Biopsy. Death. No necropsy.*

*History.*—L. S., a woman, American, single, waitress, aged 27, entered the Massachusetts General Hospital on Aug. 6, 1926, complaining of nonpainful enlargement of the glands of the neck. The patient had first noticed a tumor in the right posterior cervical region one year before entrance. Four months later, another was discovered in the left supraclavicular region, and eight months after the onset a swelling appeared under the left mandible. Three months before entry a gland appeared in the left axilla, which rapidly increased in size, only to decrease again without treatment. She lost 14 pounds (6.4 Kg.) in weight in a year.

*Examination.*—The patient was well developed and nourished. Under the angle of the left side of the jaw was a mass of several matted glands, about 5 by 3 cm.; in the left supraclavicular fossa were several glands, varying from 1 to 3 cm. in size; there were a similar, but larger, mass of glands in the left axilla, and a few small, hard glands in each groin. Blood tests revealed: 23,000 leukocytes per cubic millimeter: polymorphonuclears, 60 per cent; small mononuclears, 20 per cent; large mononuclears, 18 per cent; eosinophils, 2 per cent. While the patient was in the hospital there was slight fever, ranging from 99 to 100.5 F., and the pulse rate varied from 75 to 120.

Microscopic examination of a biopsy specimen from a gland showed a malignant lymphoma (lymphoblastoma).

*Course and Treatment.*—The patient received high voltage roentgen treatment, with relief. From 1926 to 1929 she was under observation in the x-ray treatment clinic. Metastases developed in various parts of the body, including the glands, lungs, spleen and pelvis. At times enlargement of the glands was accompanied by intolerable itching. Whenever new glands, recurrent enlargement of old

glands or roentgen evidence of metastases appeared, the patient received appropriate high voltage roentgen therapy, usually with good results.

*Subsequent Admission.*—Sept. 11, 1930, the patient returned to the hospital on account of dull, diffuse headache and because of tumors in the scalp. She had vomited several times and for one week had complained of soreness of the teeth and gums and stiffness of the jaw. On physical examination she was drowsy; many small, palpable nodules were scattered over the skull; the spleen was 3 cm. below the left costal margin. There were: partial ptosis of the right eyelid; slight fullness of both orbits, which was more marked on the right; paralysis of the external rectus and bilateral numbness of the jaws. The motor fifth nerve appeared to function normally, and the upper sensory branches were not involved. The right ankle and knee jerks were greater than those on the left.

*Subsequent Course.*—Ten days after the patient's last entrance to the hospital, she had difficulty in swallowing, with drooling of saliva, and was unable to protrude the tongue farther than the teeth. A series of high voltage roentgen treatments was given to both sides of the skull, with marked improvement of the palsies of the sixth and twelfth nerves; the fifth, however, did not respond as well. A tumor appeared in the upper right quadrant of the abdomen; this was also treated. The patient died on Nov. 22, 1930, at home. Necropsy was not permitted.

*Comment.*—The chief neurologic involvement in this case was that of the cranial nerves. The tumor responded partially to roentgen therapy. It is presumed that, on account of the depth of the lesion or possibly its infiltrating character, treatment was not so successful as in other cases.

*CASE 7.—Lymphoblastoma (pseudoleukemicum). Compression paraplegia, as the first symptom, except for root pain. Operations: cholecystectomy, followed by laminectomy. Diagnosis made only after second operation; glandular enlargement not present until two years later. Roentgen therapy. Biopsy.*

*History.*—F. S., a man, aged 63, married, Portuguese, a furniture finisher, entered the Massachusetts General Hospital on March 18, 1930, with an indefinite history of intermittent, shooting pain in the right side of the chest along the costal margin. Several months before entrance he had been jaundiced, and the presence of gallstones was demonstrated by roentgenologic examination. An operation had been performed at another hospital; gallstones were found and removed. The pain continued in spite of the operation, and the patient next noticed weakness of the legs. Five weeks after operation, he complained of a "pins and needles" sensation in both legs, and the weakness had become more marked. Five days before entry, motor and sensory paralysis of both legs developed, with sphincteric weakness.

*Examination.*—Neurologic examination showed: paresis of the legs, with ability to move the right ankle and toes slightly and the left leg as a whole; the right knee jerk and ankle jerk greater than those on the left; a bilateral Babinski sign; partial loss of sensation to the level of the seventh thoracic cord segment.

Lumbar puncture on March 19, 1930, showed that the spinal fluid was clear and slightly yellow; the initial pressure was 70; there was a rise on jugular compression to 90 and a drop on release to 70; after withdrawal of 5 cc., the pressure was 30; after withdrawal of 7 cc., 0; the cells numbered 5 per cubic millimeter; the total protein was 166 mg. per hundred cubic centimeters; the colloidal gold curve was 0111122211; the Wassermann test was negative.

The Wassermann test of the blood was negative and examination of the urine gave negative results. Examination of the blood revealed: 11,600 white cells per cubic millimeter; hemoglobin, 55 per cent; red cells, 3,650,000 per cubic millimeter; a differential count, except for 9 per cent of eosinophils, was normal.

*Operation and Course.*—Three days after entrance, a laminectomy of the third, fourth, fifth and sixth dorsal vertebrae was done by Dr. W. J. Mixer. Beneath the fourth and fifth laminae an irregular, granulating mass 2 by  $\frac{3}{4}$  by  $\frac{1}{4}$  inches in size, compressing the spinal cord from outside the dura, was found. There was no involvement of the bone. The compression was relieved.

Microscopic examination of the tissue showed lymphoblastoma.

On April 9, 1930, nineteen days after the operation, a note was made that sensation in the patient's legs had returned on the second day after the operation and motion, on the fourth. Another lumbar puncture showed no evidence of block. There was slow but progressive return of motion throughout the patient's stay in the hospital. Physical examinations, made before the patient was discharged, did not show any other evidence of lymphoblastoma. High voltage roentgen treatment was administered to the thoracic spine, centered over the sixth dorsal vertebra.

On April 16, 1932, there was marked improvement in gait; the patient walked with almost no ataxia. He complained of some pain low in the back, but his general condition was good. The deep reflexes in the legs were active; there was no Babinski sign or clonus. Sensation had returned to normal. The sphincters were functioning well. Two days later, physical examination disclosed three or four small, shotty glands in each axilla, with four or five glands in the groins, and above Poupart's ligament, on each side, was a gland of similar size. The lungs were clear. The spleen was barely palpable in the left flank. It was thought that the presence of new glands and a palpable spleen, two years after operation, was evidence verifying the original pathologic diagnosis of lymphoblastoma.

*Comment.*—This case illustrates the commonest type of the lymphoblastic tumors so far as they affect the central nervous system. Compression paraplegia with rapid onset is often the first symptom noted. Laminectomy appears to be an emergency operation, and it is difficult, without other evidence of disease, to prevent the surgical relief of the pressure. From experience with tumors elsewhere one could postulate that an equally good result might be obtained by roentgen therapy, and this should be the method of choice in cases in which the diagnosis can be made. In this case clinical confirmation of the pathologic diagnosis was not possible until nearly two years after the onset.

#### CONCLUSIONS

1. Lymphoblastoma is a convenient group designation for all tumors the cell type of which is the lymphoblast, the precursor of the adult lymphocyte.
2. The term includes its leukemic and aleukemic forms, Hodgkin's disease, lymphosarcoma, pseudoleukemia and mycosis fungoides.
3. All types of lymphoblastoma may cause compression of the central nervous system. Actual invasion of the nervous system or meninges may take place.

4. Multiple neurologic symptoms and signs may be present, sometimes early in the course of the disease.

5. Lymphoblastomatous lesions, either compressing or infiltrating the nervous system, respond to roentgen therapy in the same manner as lesions in other parts of the body. Treatment should be given promptly, however, in view of the deleterious effects of long-continued pressure or infiltration on nervous tissue. Our best results were obtained when treatment was given shortly after the localizing diagnosis was made.

6. Neurologic symptoms may be relieved by appropriate roentgen treatment, and occasionally life may be prolonged.

7. Seven cases, in two of which the diagnosis was confirmed at necropsy, are reported to illustrate the aforementioned points.

#### ABSTRACT OF DISCUSSION

DR. GEORGE W. HOLMES, Boston: If one uses the classification Drs. Viets and Hunter have suggested, this disease immediately becomes a general disease. Physicians are apt to think of it as a localized disease and as a disease in which the presenting lesion is in the glands of the neck, whereas it often appears in some part of the nervous system or in the gastro-intestinal tract. Perhaps the secret of successful diagnosis in this disease is in keeping this in mind.

As to radiation therapy and the importance of having accurate localization, most of our failures have occurred when we have not had the advantage of a careful examination by a neurologist with successful localization of the lesion. In the treatment of the neurologic conditions, there should be prompt application of a sufficient amount of radiation to bring about reduction of the tumor; otherwise permanent damage will result. It makes very little difference whether the radiation from radium or that from the roentgen ray is used. These tumors are extremely sensitive, and it is not necessary to use doses large enough to injure normal tissue. They are usually quite widely distributed, and the use of radium in the form of seeds or in small needles is usually successful. I think that the radium pack or high voltage roentgen rays are the best instruments. The necessary dose in most cases is not over half the erythema dose, provided the proper kind of radiation is used. The treatment can be carried out over long periods without any evidence of injury to the skin.

There is a necessity for careful check-up with the internist before treatment and in selection of the number of treatments. We must remember that the treatment is a palliative measure, not a cure, and we should not irradiate the patient's whole body in an attempt to eliminate the disease. We should treat each symptom as it arises, giving as little treatment as necessary to bring about relief. Otherwise the patient's life may be shortened rather than prolonged.

DR. FRANK J. HECK, Rochester, Minn.: As Dr. Holmes has pointed out, because of the wide distribution of the reticulo-endothelial system, it is easy to understand the great variety of symptoms which may arise from its involvement. I believe that if neurologic involvement were looked for, it would be found in a larger percentage of cases than is ordinarily pointed out in the literature. This is more evident at necropsy. Neurologic involvement will be found in a high percentage of cases, even though neurologic signs or symptoms may not have been apparent before death. The late involvement of the central nervous system by lymphoblastoma leukemicum is illustrated by one case in this paper. The long

duration of cases of this type would certainly afford every opportunity for involvement of the nervous system, since not infrequently lymphatic leukemia may last from five to ten years, and cases of twenty years' duration have been reported.

The retina is involved in myelogenous leukemia much more frequently than in the lymphatic type. Although in the lymphatic type actual infiltration is rarely seen, in the myelogenous type leukemic infiltrates were seen in ten of seventy-two cases in which examination was made. In 1927 Troemner and Wohlwill demonstrated involvement of the central nervous system in eight of nine cases of myelogenous leukemia. In only two were there neurologic symptoms of note.

The occasional coincidence of a cerebral lesion and leukemia may be seen. At the Mayo Clinic we have recently had a case belonging to the type of lymphoblastoma aleukemicum, in which marked enlargement and destruction of the sella turcica was found, but with few neurologic signs. Aside from bilateral contraction of color fields, examination gave negative results. Although it is unlikely that the leukemia was responsible for the changes in the sella turcica, roentgen treatment, if used early, should be an aid in diagnosis.

DR. GEORGE HASSIN, Chicago: I was very much interested in a slide which showed an intense infiltration of the subarachnoid space. This is properly diagnosed as aseptic meningitis, the majority of the infiltrating cells having, of course, been those of the lymphoblastoma rather than the meningeal inflammatory cells. The point is that, in spite of the enormous infiltration of the subarachnoid space, hardly any of its cells invaded the subjacent brain tissue. This obtains also in septic conditions of the subarachnoid spaces of the brain and cord. They do, however, invade the parenchyma if abnormal conditions arise in the subarachnoid spaces, when they are overcrowded with cells, for instance. From this point of view the slide I think is very important.

Another feature of interest, but hard to understand, is how the lymphoblasts reach the subarachnoid space; that is, from where did they come?

DR. HENRY R. VIETS, Boston: The point that Dr. Holmes made of giving repeated roentgen therapy when symptoms arise is a most important one, as some of the patients with this condition have been treated for as long as fifteen or eighteen years. The treatment consists of watching the patient and, when symptoms arise indicating a localized lesion, administering appropriate therapy. That is the most important clinical point that can be made.

In regard to the pathology, I did not go into the details. The patient Dr. Hassin speaks of, the one with meningeal infiltration, had numerous signs of disease elsewhere in the body; I have no idea of exactly the course taken by this tumorous tissue into the subarachnoid space.

## REACTION OF CEREBRAL TISSUE TO DIRECT INJECTION OF OIL

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AND

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The reactions of neuroglia and of microglia in cerebral trauma have been well studied in the last few years, but the changes produced by the direct introduction of foreign fluid substances have received little attention. Carmichael,<sup>1</sup> in 1928, injected rabbit's blood into the brains of rabbits in order to show the development of its phagocytosis. Davidoff, Seegal and Seegal,<sup>2</sup> in a study of the Arthus phenomenon, injected foreign proteins into the brains of sensitized rabbits to demonstrate the same cellular reaction in the brain that is found in the skin.

The present work was undertaken in order to study the cerebral reaction in rats and rabbits when rabbit fat, mineral oil or olive oil was introduced directly into the brain substance.

### METHOD

At first an attempt was made to dye olive oil with sudan 4, neutral red and trypan blue so that it could be more easily recognized microscopically, but the dye invariably proved too toxic; so only unstained oil could be used. The operations were performed under aseptic conditions. A small hole was bored into the skull, and 0.5 cc. of sterile oil or fat was injected into the brain substance. Since in rats there was a large mortality and the staining for microglia was unsatisfactory, only rabbits were used. Three rabbits appeared to recover from the operation, but died in convulsions from two to forty-eight hours later. Eleven rabbits survived the operation, and were killed at intervals of from twenty-four hours to fifty-one days after the injections.

When the skulls of the animals were opened, oil flowed freely from the cerebral surfaces, along the cranial nerves and, on section, from the ventricles. Blocks of the brains were fixed in formaldehyde-ammonium bromide solution and stained with the usual stains for microglia and neuroglia, combined also with sudan 4.

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From the Pathology Laboratory of the Buffalo General Hospital.

1. Carmichael, E. A.: Microglia: An Experimental Study in Rabbits After Intracerebral Injection of Blood, *J. Neurol. & Psychopath.* **9**:209, 1928.

2. Davidoff, Leo M.; Seegal, B. C., and Seegal, David: The Arthus Phenomenon. Local Anaphylactic Inflammation in the Rabbit Brain, *J. Exper. Med.* **55**:163, 1932.

## OBSERVATIONS

*Phagocytosis of the Oil.*—The type of oil injected is not specified in the various descriptions, because in the microscopic preparations each oil or fat used was stained bright red with sudan 4 and produced the same type of cellular response. Large and small globules of oil were found lying free in the meninges and ventricles as late as fifty-one days after the injection. In these areas macrophages were rarely seen absorbing the oil until the tenth day, and then only in small numbers. Twenty-two days after the injection, large macrophages filled with oil were present around the entire circumference of the ventricles, while the number of macrophages in the meninges had increased only slightly since the tenth day. On the forty-third and fifty-first days macrophages in the meninges were also few, while in the ventricles the number had decreased since the twenty-second day. However, as the amount of successfully injected oil varied with each brain, no conclusions can be drawn concerning the time factor in regard to the amount of oil absorbed. In each wound oil globules were present, except in the one which was healed on the fifty-first day following the injection. How much oil was absorbed from the wounds and how much was washed out by the spinal fluid it is impossible to conclude, since the fat of the destroyed nerve tissue in the fat granule cells was stained the same bright red with sudan 4 as the injected oil. No oil or fat was ever found in the neuroglia or ganglion cells. However, the oil must have been absorbed directly or indirectly since fat-staining fluid was present in the vessels of the brain of the rabbit killed on the forty-third day. These vessels were in the meninges, in the white substance, particularly that of the cornu ammonis, and in the lower part of the gray substance, while the vessels and the capillaries of the upper part of the cortex were free. Neither perivascular cellular reaction nor perivascular demyelination was demonstrable around these vessels. It was impossible to know when the oil may have been absorbed into the blood, since the visceral organs were free from oil, and only a few macrophages of the lungs contained lipoid-staining granules. A few capillaries of the lungs showed the same lipemic stain that was found in the vessels of the brain.

*Reactive Growth of the Oligodendroglia Produced by Injection of Oil.*—In the first twenty-four hours, blood and oil filled the wound, which penetrated the gray and white substance to the ependymal edge. At this time, the oligodendroglia at the margin of the wound were swollen to large round cells, the nuclei of which were broken into two or four parts similar to the nuclei in polymorphonuclear leukocytes; the cyto-



Fig. 1.—Seventeen day wound showing glia in both radiating and parallel formation. The wound is open except for connective tissue in the cortical and ependymal parts.



Fig. 2.—Stripped capillaries on the border of a twenty-four hour wound.

plasm of the former cells, however, was greater in amount. Sections of later wounds revealed no evidence that the oligodendroglia produced fat-granule cells of ingested oil or took part in scar formation.

*Reactive Growth of the Astrocytes Produced by Injection of Oil.*—A partial loss of processes, slight swelling and disintegration characterized the reaction of the astrocytes at the margin of the wound during the first twenty-four hours. Those in the vicinity of the wound stained poorly. After four days the wound was surrounded by numerous cells, which were not stained by the method of Cajal. Contiguous to the unstained cells was a layer of hypertrophic astrocytes, in both the gray and the white substance. The hemorrhage had almost disappeared, leaving only oil inside the injured area. On succeeding days hypertrophic glia increased in the surrounding nerve tissue and at the margin of the wound. One wound made in the white substance ran parallel to the gray substance. A heavy growth of hypertrophic glia with thick processes extended downward from the gray substance at right angles to the wound. Likewise in the white substance the glia were as large and as numerous as those in the gray substance, but were irregularly formed about the wound. On the tenth day the two zone growth was no longer evident. The proliferation of the astrocytes had somewhat lessened in the adjacent tissue, but had become pronounced in the gray and in the white substance immediately surrounding the partially open wound. Other specimens taken farther from the center of this injured area showed fewer glia reacting to the wound. In all sections of this brain the astrocytes nearest the wound were the most distinctly hypertrophic and showed both parallel and radiating formation. Seventeen days after the operation, a few hypertrophic glia were found, chiefly in the periphery of the open wound, where they conformed to no particular type of formation. In the wound of twenty-two days' duration, the oil had penetrated only the gray substance in the midline, producing a triangular hollow wound surrounded by a moderately dense growth of hypertrophic glia. A second injection into this brain had been made fifteen days previously; it was made into the gray substance, where it produced a round open wound surrounded by hypertrophic glia in a radial cicatrix. Hypertrophic astrocytes were also found around the ventricle, particularly near the wounds. After fifty-one days a straight line of hypertrophic astrocytes closed the injured area, which extended to the ventricles. So little indentation of the molecular layer had occurred that the scar was found with difficulty.

*Reaction of Connective Tissue to Injection of Oil.*—The connective tissue and the capillary growth varied as greatly as did the neuroglia.



Fig. 3.—Adventitial wall cell in the perivascular space of a vessel near a twenty-four hour wound.

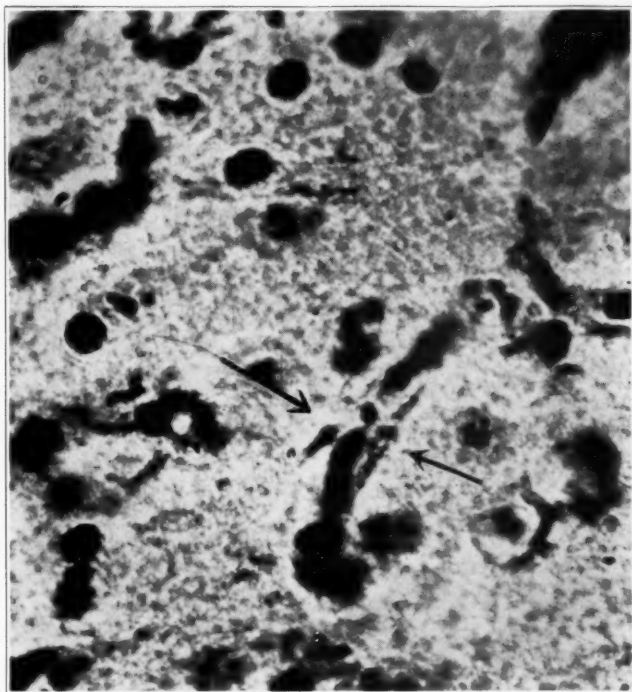


Fig. 4.—Two early migrated adventitial wall cells at the edge of the perivascular nerve tissue of a capillary at the border of a twenty-four hour wound.

In three to five day wounds, there was a sprouting of the capillaries along the margin of the wound in the cortex. At ten days, partially formed connective tissue was present in the wound, but only in the gray substance. This tissue was not connected with the dura mater, and was connected only lightly with the meninges. Other sections of this wound showed an oval empty space below the molecular layer of the cortex. In the wound of seventeen days' duration, a free mass of connective tissue, apparently unattached, was found at the margin of the molecular layer. One section showed connective tissue strands in both the cortical and the ependymal parts of the wound. The wound of fifty-one days' duration was closed with only a few fine connective tissue fibers.

*Reaction of Microglia to Injection of Oil.*—The capillaries nearest the wound were stripped of microglia twenty-four hours after the injection of oil. Migrated microglia were found in and around the wound in early and late phagocytic forms; the processes of the latter were swollen around globules of fat. Beyond the stripped capillaries an increased number of microglia were present. These were observed on the capillaries, around the blood vessels and in the intervening spaces. On the succeeding days fat granule cells became numerous until the sixth and seventh days, when a diminution took place. Few fat granule cells were found in the wound of ten days' duration, and none in the seventeen day wound. However, the wound of twenty-two days showed numerous fat granule cells containing blood pigment. No fat granule cells were present in the fifty-one day wound.

The most distinctive feature of the Hortega preparations was the clearness with which the relation of the microglia to the blood vessels was demonstrated. It was evident that microglia developed from adventitial wall cells. The earliest stage of this transformation was the budding of the adventitial wall cells from the capillaries. This was characterized by a bulging of a nucleus and by a faint impregnation of the long, narrow cytoplasm with the silver stain in contrast to the unstained cytoplasm of the other cells of the capillaries. Such bulgings were increased in number near wounds of twenty-four hours' duration and as late as the third day. The entire cell was seen to bulge progressively, until in the final stage the elongated cell, still faintly stained, was found in the narrow area between the capillary wall and the nerve tissue.

Budding of the adventitial wall cells from the larger vessels was not seen. The presence of adventitial wall cells in the perivascular spaces of the blood vessels was always demonstrable, not only near wounds but in the vessels leading down from the meninges. The



Fig. 5.—An early migrated adventitial wall cell on the edge of the perivascular nerve tissue of a vessel near an area of parasitic encephalitis. The cell shows faintly staining bipolar cytoplasm.

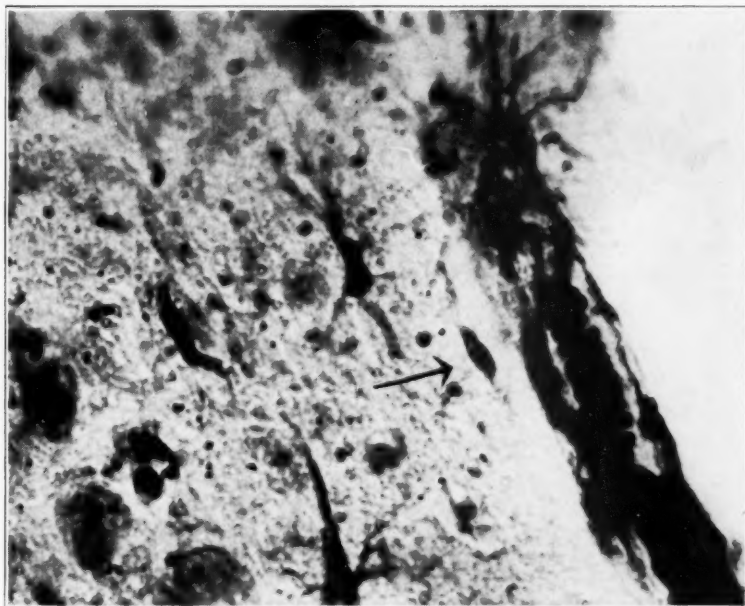


Fig. 6.—An early migrated adventitial wall cell at the edge of the perivascular nerve tissue of a vessel near a two day wound. The cell shows faintly staining bipolar cytoplasm.

adventitial wall cells in the perivascular spaces were the marked feature in the area surrounding a twenty-four hour wound. They were present in increased numbers around both the blood vessels and the capillaries, particularly capillaries stripped of microglia at the margin of the wound. Not only was there a proliferation of the adventitial wall cells in the perivascular space, but some of these cells had already attached themselves to the nerve tissue at the edge of the perivascular space, especially around the capillaries at the margin of the wound. On both sides of one such capillary, adventitial wall cells were lying partly on the nerve tissue and partly in the perivascular space. These cells were distinguished from those inside the perivascular spaces only by the slightly greater affinity of their cytoplasm for silver; otherwise, their nuclei and elongated cytoplasms were similar to those of the adventitial wall cells. The chief characteristics at the margin of the twenty-four hour wounds were, therefore, the proliferation of adventitial wall cells into the perivascular spaces and the slightly changed adventitial wall cells at the edge of the nerve tissue. No maturing migrated cells were seen at the edge of the nerve tissue in this area. In sharp contrast to the twenty-four hour wounds, it was difficult to find adventitial wall cells in the perivascular spaces in and about three and four day wounds. But in these later wounds the number of newly attached cells was pronounced, while even more distinctive was the number of maturing forms at the edge of the nerve tissue.

The migration of adventitial wall cells was demonstrated not only about wounds, but in an infiltrated vessel near an area of parasitic encephalitis. In the round cells of the perivascular space of this vessel there was an open break from which an adventitial wall cell had apparently just migrated to the nerve tissue. The cytoplasm of this cell, like that of the cells already described, was elongated and narrow, without processes, and stained faintly; the nucleus, like the cytoplasm, was similar to that of adventitial wall cells. Other narrow, elongated cells without processes were seen at the edge of the perivascular nerve tissue about the vessels in normal-appearing parts of the brain, near foci of parasitic encephalitis, and about wounds after from three to seven days. These cells were more deeply impregnated with silver and suggested a longer attachment to the nerve tissue. A still later stage of growth of the cells was found near five to seven day wounds. Such cells showed short, faintly stained processes developing from the cytoplasm at the terminal end, and were typical of young perivascular bipolar cells.

Slightly immature microglia can migrate from the perivascular nerve tissue. This was evident from the presence of bipolar cells in the

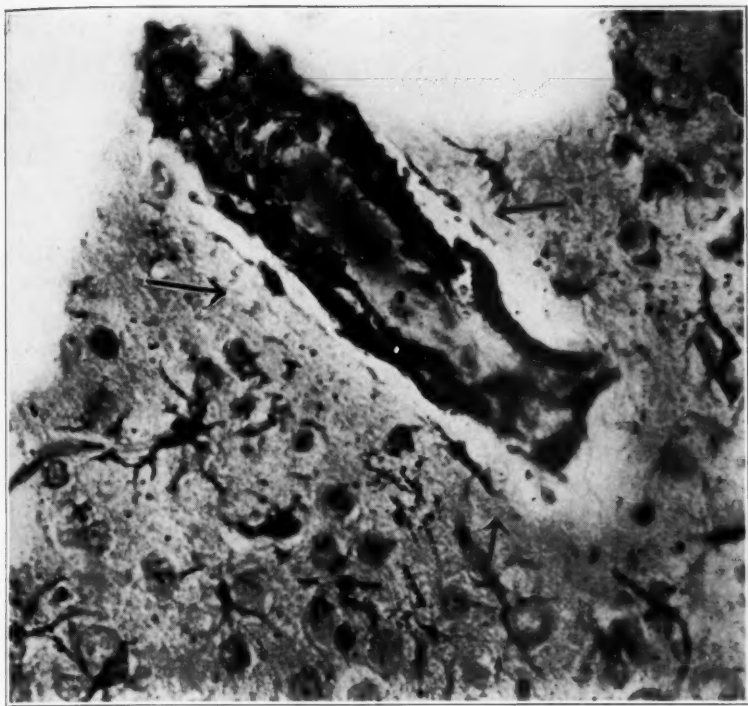


Fig. 7.—Older migrated adventitial wall cells at the edge of the perivascular space with fine processes growing from the poles, in a vessel near a five day wound.

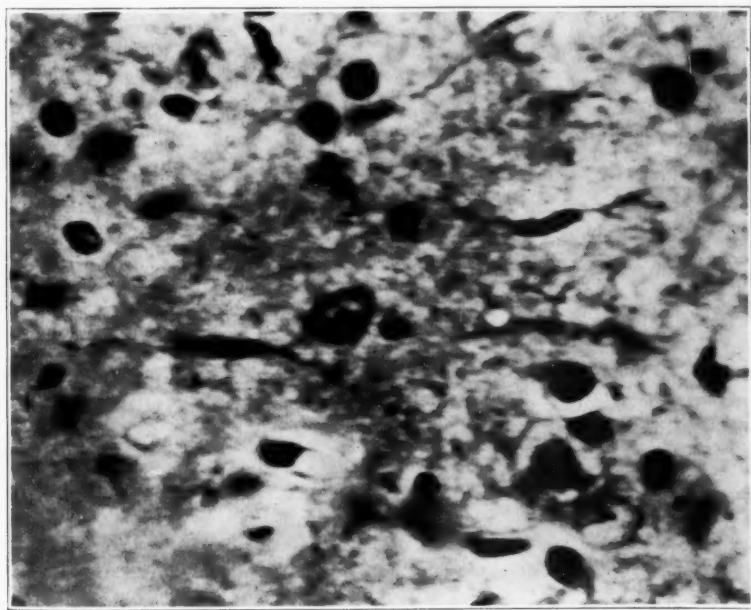


Fig. 8.—Immature bipolar microglia in the nerve tissue at the outer edge of a five day wound.

nerve tissue on the outlying edge of the five and seven day wounds. Early multipolar cells in the perivascular nerve tissue were also seen. These cells showed faintly stained processes, growing from the cytoplasm about the nucleus and from both poles. The last stage of microglial development was evident everywhere in the fully grown multipolar microglia with deeply stained processes at the edge of the perivascular spaces. It is significant that division of microglia in the branching form was never seen. Likewise, the most immature forms of microglia, that is, those having no processes, were seen only at the edge of the perivascular spaces, never in the nerve tissue.

*Reaction of Neuroglia and Microglia to Injections of Trypan Blue and Oil.*—Three rabbits were given injections of 10 cc. of a 1 per cent solution of trypan blue every day for three days prior to the injection of oil. One rabbit died twenty-four hours after the injection. There was slight meningitis, but nothing resembling the Arthus phenomenon. A second rabbit received two additional injections of trypan blue after the operation and was killed on the fourth day. On gross examination, the wound, the meninges, the choroid plexus and the cornu ammonis were stained blue. Microscopic sections were stained with aluminum carmine, which clearly showed small particles of dye in the cells of the choroid plexus, in the microglia beneath the meninges and the ependyma, in the perivascular spindle and round cells and in the fat granule cells.

The microglial and the neuroglial reactions to the injected oil in this wound of four days' duration were similar to those in wounds of the same duration in rabbits into which trypan blue had not been injected. After the introduction of oil the third rabbit received, during a period of two weeks, seven more injections of trypan blue, and died on the forty-third day. Gross and microscopic examination showed that the dye had almost disappeared from the brain, except in the cells of the choroid plexus and meninges and in the fat granule cells of the wound, while the visceral organs were deeply stained. The cerebral wound was large, extending in an irregular line from the cortex of the frontal lobe through the cornu ammonis. It was partially closed in the cortex but was both open and closed in the cornu ammonis. Throughout its entire extent the microglia and fat granule cells were as numerous as in a three day wound. Scattered hypertrophic astrocytes were present for a considerable distance about the injured area, and were closely packed around the entire ventricle on that side. The capillaries were few in the cortical wound, and for the most part grew parallel to it. In the cornu ammonis and the lower part of the white substance the capillaries were numerous, branching in all directions.

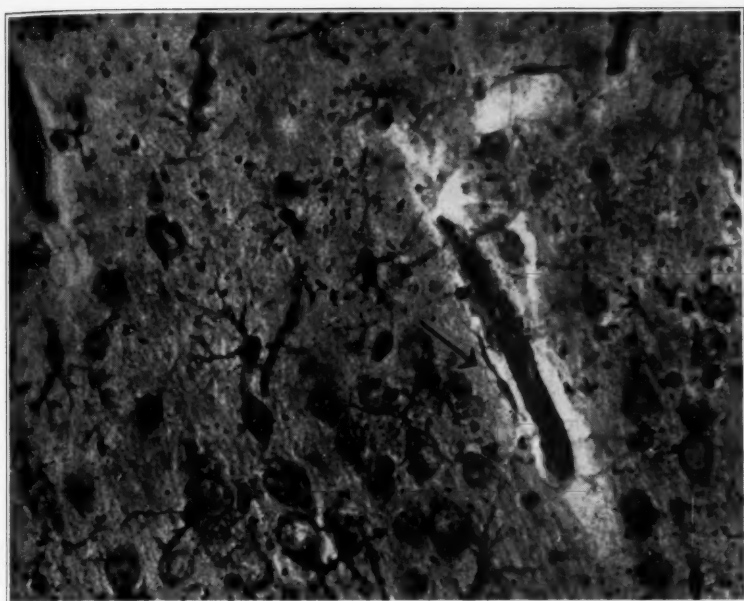


Fig. 9.—Maturing microglia or adventitial wall cells at the edge of the perivascular space, with fine filaments growing from both poles and central cytoplasm.

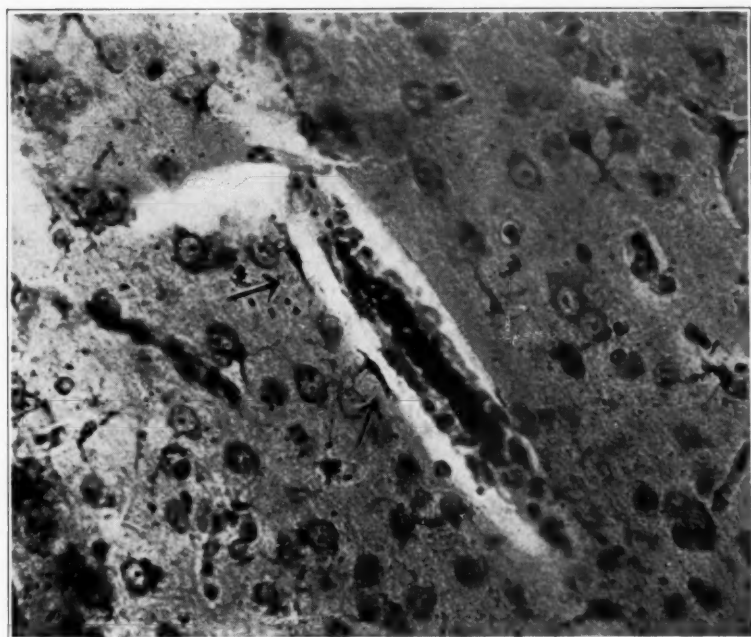


Fig. 10.—Mature microglia at the edge of the perivascular space.

## COMMENT

In 1919 and 1921, Hortega<sup>3</sup> published his work concerning the origin and methods of staining of the microglia. He concluded that these cells are of mesodermal origin, in contrast to the neuroglia, which have an ectodermal derivation. Since that time controversy has waged regarding the justification of that conclusion. But even the admission that the microglia are mesodermal has evoked numerous suggestions as to their site of origin. Penfield<sup>4</sup> apparently agreed with Hortega that the microglia are first seen in the undersurface of the cerebral peduncles and beneath the ependyma, where the tela choroidea is formed. He stated, however, that he has never observed the transition from pial fibroblasts into microglia. Penfield likewise considered that microglia may develop from the adventitia of larger cerebral vessels and also from polyblastic cells, which are, however, adventitial cells. Wells and Carmichael<sup>5</sup> obtained microglia-like cells from tissue cultures of brain substance containing blood vessels. They thought that these microglia-like cells developed from the blood vessels, because these cells were absent in blood vessel-free tissue. Kubie<sup>6</sup> succeeded in staining only perivascular clasmotocytes (in our nomenclature, adventitial wall cells) and lymphocytes by the supravital technic in pieces of brain in young and adult animals. But since some of the clasmotocytes were free from the vessel wall, possibly by accident, he suggested that the clasmotocytes might wander into the nerve tissues and take on processes, provided there was no impenetrable barrier.

In the present study the perivascular spaces were sufficiently wide to render a clear picture of the wandering of the adventitial wall cells to the nerve tissue and of their transformation into microglia with processes. It can, of course, be questioned whether the cells clinging to the edge of the nerve tissue are immature microglia without processes of mature microglia with unstained processes. The latter seems improbable, since in the surrounding tissue the processes of the other microglia are distinct; furthermore, the difference in size of the newly attached immature cells and of the mature microglia is apparent, whereas the similarity of their morphology is evidence of their relationship. These small clinging cells might also be considered early phagocytosing cells which have lost their processes, but the cytoplasm is not swollen.

3. del Río-Hortega, P.: El tercer elemento de los centros nerviosos, *Bol. Soc. españ. de biol.* **9**:154, 1919; *Mem. r. Soc. españ. de hist. nat.* **10**:213, 1921.

4. Penfield, W.: Microglia and the Process of Phagocytosis in Gliomas, *Am. J. Path.* **1**:77, 1925.

5. Wells, A. O., and Carmichael, E. A.: Microglia, *Brain* **53**:1, 1930.

6. Kubie, L. A.: Study of Perivascular Tissues of Central Nervous System with Supravital Technique, *J. Exper. Med.* **46**:615, 1927.

Such immature cells might seem to come from the nearby microglia, but no evidence of division was found. On the other hand, the similarity of these cells to adventitial wall cells in morphology and in staining is unmistakable, since both have lightly stained, narrow, elongated cytoplasm and variously shaped nuclei. They cannot be related to the oligodendroglia or to the macroglia by any likeness of staining or morphology, but can be linked only with the similar adventitial wall cells and with the microglia, which they grow to resemble on the edge of the perivascular space. That a growing maturity of the newly attached adventitial cell occurs is apparent not only from the development of faintly stained, barely perceptible, fine filaments of young processes but from the contrast of the early processes to the neighboring deeply stained processes of mature microglia.

Likewise, it seems evident that new microglia are formed from adventitial wall cells, since near twenty-four hour wounds the capillaries are stripped of mature microglia and numerous spindle cells are found in, and at the edge of, the perivascular spaces. It would appear, therefore, that the migration of mature microglia from the capillaries instigated a reproduction of adventitial wall cells to fill their places. Furthermore, near the three and four day wounds adventitial wall cells were few, while the mature forms of attached cells were abundant. Since the latter are lacking in the twenty-four hour wounds, it would seem to imply that mature forms of microglia have not had sufficient time to develop. Penfield<sup>4</sup> thought that microglia in the late stages of phagocytosis migrated to the vessels, gave up their contents and returned to their original form of early phagocytic activity. However, it is known that the fat granule cells retrograde by karyorrhexis; therefore, the early phagocytic forms of microglia about the blood vessels are probably not in the process of renewing their activity but are newly developed cells undergoing phagocytic change. Carmichael<sup>1</sup> suggested that since many microglia appeared at the bifurcation of the capillaries, the microglia might originate there. In this series microglia did not appear to be more numerous at the bifurcation of capillaries than elsewhere.

The reaction of astrocytes to injected oil appears to be similar to their behavior when blood is introduced into the brain, as has been described by Carmichael.<sup>1</sup> That is, the hypertrophic glial response to blood was as well developed in three days as it was in a similar period after the injection of oil. Likewise, a walling off of the injured area was accomplished by the astrocytes in fifteen days as compared to seventeen days in our series. In contrast to this early reaction of astrocytes to directly injected fluids was a more delayed one obtained by

stab and hollow wounds in the experiments of Linell.<sup>7</sup> According to him, at the end of six days the astrocytes in both types of wound were in the same stage of increased size and number as was found by both Carmichael and ourselves at three days. The walling off of the stab wound with a reduction of the astrocytes did not occur until the twenty-eighth day, whereas the astrocytes were still proliferating in the hollow wound at about the stage of the twenty-first day of the stab wound. These results appeared to Linell as some confirmation of Penfield's<sup>8</sup> belief that the presence of destroyed brain substance in a wound stimulates glial growth. The rapid walling off of the wounds in our experiments would suggest that the addition of a foreign substance with destroyed brain tissue excites an early response of glia and an equally early cessation of glial growth.

One distinction that Penfield<sup>8</sup> made between open and closed wounds was in regard to the astrocytes, which he described as sending their processes in parallel formation about cannular wounds and in radiating formation about stab wounds. This division of astrocytes cannot be confirmed in this series, since both types of glial formation were found in stab wounds which showed both open and closed tracts. Linell<sup>7</sup> also found both types of glial formation in stab wounds. Although the injection of oil tended to produce closed wounds with capillary growth, the line of closure in one wound after fifty-one days was straight, with few strands of connective tissue. Gliosis was not evident, and little indentation of the molecular layer was present. These results are surprising since, as Penfield<sup>8</sup> has demonstrated, it is the removal of the destroyed brain substance that prevents the formation of new capillaries, connective tissue and gliosis. In this wound not only was the injured brain substance not removed, but foreign material was added. The closure of this wound was, of course, to be expected, since, according to Penfield,<sup>8</sup> it is the cannular wounds that remain open.

A glial reaction in the white substance was not found by Penfield<sup>8</sup> in any wound, but was mentioned by Linell.<sup>7</sup> In our experiments the increase in number and in size of the glia in the white substance around all the wounds and also around two oil-filled ventricles suggests an activity of the astrocytes other than the formation of cicatrix.

The results of gross examination of the brain of the rabbit which had been given free injections of trypan blue corresponded for the most

7. Linell, E. A.: The Histology of Neuroglial Changes Following Cerebral Trauma, *Arch. Neurol. & Psychiat.* **22**:926 (Nov.) 1929.

8. Penfield, W., and Buckley, R. C.: Punctures of the Brain, *Arch. Neurol. & Psychiat.* **20**:1 (July) 1928.

part to the description given by Macklin and Macklin<sup>9</sup> of rabbits injured by stab wounds and given three injections of trypan blue. Blueness of the cornu ammonis, which was found in our animals, was not mentioned by them, but was described by Wells and Carmichael<sup>5</sup> who gave injections to rabbits over a longer period. They also found blueness of the cortex and basal ganglia. On microscopic examination, Macklin and Macklin<sup>9</sup> found particles of dye in the cells along the blood vessels, in the macrophages of the meninges, in the cells of the choroid plexus and in the macrophages in and around the wounds. Russell<sup>10</sup> repeated their work, but made silver carbonate preparations for microglia. She found particles of dye in phagocytosing microglia, fat granule cells and vessel wall cells. Since the phagocytosing microglia absorbed particles of dye, she believed that they were part of the reticulo-endothelial system. In uninjured rabbits subjected to many injections of trypan blue, Wells and Carmichael<sup>5</sup> were able to find particles of dye in microglia around ganglion cells of the cortex, of the basal ganglia and of the cornu ammonis and in the cells of the vessel walls. They used aluminum carmine preparations, since by the silver carbonate stain it was impossible for them to find particles of dye in the microglia. It was their conclusion that the absorption of dye by the microglia proved the relationship of these cells to the reticulo-endothelial system. They did not mention particles of dye in the microglia beneath the ependyma or in the molecular layer under the meninges, as described by us. None of these observers discussed the importance of the fact that in the brain substance particles of dye are absorbed only by the microglia and by the adventitial wall cells.

Our study of animals given injections of trypan blue was made in order to observe whether the presence of the dye in the phagocytic cells prevented the usual microglial and neuroglial response to the injection of oil in the brain. In the four day wound, no unusual reaction of the microglia and neuroglia to the injection of oil was noted. However, the wound of forty-three days' duration showed little healing. Therefore, it seems possible that the adventitial wall cells and microglia had been so plugged with dye and the fat granule cells still contained so much dye that the removal of fat and oil was delayed. Also, a sluggish circulation due to the toxicity of the dye may have failed to absorb the fat and oil. On the other hand, the wound in the cornu ammonis might have been the result of embolic softening rather than of the injection of oil except that the usual vascular reaction around

9. Macklin, C. C., and Macklin, M. T.: Brain Repair, *Arch. Neurol. & Psychiat.* **3**:313 (Feb.) 1920.

10. Russell, D. S.: Intravital Staining of Microglia with Trypan Blue, *Am. J. Path.* **5**:451, 1929.

areas of softening was lacking. As to the final disposal of the oil, it is evident from the phagocytic cells of the ventricles and of the meninges that the oil must have been absorbed by the blood vessels. The lipemic state of the vessels of the brain and the lungs of the rabbit given injections of trypan blue suggests further that the oil is absorbed. The preponderance of the oil in the vessels of the white substance of the brain is perhaps explained by the small number of capillaries in the white substance as compared with the great system in the gray substance.

#### CONCLUSIONS

Wounds produced by the direct injection of oil into the brain substance tend to close with the formation of little connective tissue. The early growth of the macroglia in walling off the area of injury produced by the injection of oil is more rapid than in stab or hollow wounds and shows both parallel and radiating formations. The microglia show the usual response to injury. The oligodendroglia present no reaction except during the first twenty-four hours, when they show a loss of processes, a swelling of the cytoplasm and a nuclear change.

The injected oil is apparently absorbed into the blood.

The experiments failed to show evidence that either neuroglia or ganglion cells absorb fat and oil. This suggests that the lipid content of ganglion cells and glia cells in diseases and in senile changes is not due to absorption of lipoids.

The subcutaneous injection of trypan blue over a long period apparently delays or hinders the phagocytosis of injected oil and destroyed brain substance.

The transformation of adventitial wall cells into microglia has been demonstrated.

# PAROXYSMAL LACRIMATION DURING EATING AS A SEQUEL OF FACIAL PALSY (SYNDROME OF CROCODILE TEARS)

REPORT OF FOUR CASES WITH A POSSIBLE INTERPRETATION AND  
COMPARISON WITH THE AURICULOTEMPORAL SYNDROME

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My purpose in this paper is to draw attention to an interesting phenomenon which has been observed in four cases of facial paralysis of peripheral type. In each case the paralysis was complete and persisted for several months. Regeneration of the nerve and return of power in the face were accompanied by facial contracture and abnormal associated movements. Coincidentally with the return of voluntary movement, excessive lacrimation on the affected side appeared whenever the patient ate or even took any sapid substance into the mouth. This phenomenon never appeared under other circumstances. It may be said at once that this symptom bears no relation to the common overflow of tears from the affected eye during the early stages of facial palsies when the lower lid is relaxed and the punctum of the tear duct is everted. Under such circumstances the tears collect in the culdesac of the conjunctiva and eventually flow over the lower lid, since they cannot reach their proper channel. The condition described in this paper does not develop until the paralysis has disappeared and the lid is again in its normal position. Moreover, it is not constant but paroxysmal and invariably associated with salivation. In each case occlusion of the lacrimal duct was ruled out.

Medical literature contains few references to this condition. In 1926 Bogorad<sup>1</sup> described a case in which lacrimation occurred during eating as a sequel of facial palsy. This he termed the *Syndrome der Krokodilstränen*, for the crocodile was formerly believed to weep hypocritical tears while devouring its victims. Kroll<sup>2</sup> mentioned a similar case. He had little to say about the cause of the syndrome, observing merely: "Es tritt hier vielleicht auch ein phylogenetisch alter Mechanismus auf dem anatomische Verbindungen zwischen den Kernen des Hirnstammes

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1. Bogorad, F. A.: Das Syndrom der Krokodilstränen, *Vrach. delo* **11**: 1328, 1928; cited by Kaminsky.<sup>3</sup>

2. Kroll, M.: Die neuropathologischen Syndrome; zugleich Differentialdiagnostik der Nervenkrankheiten, Berlin, Julius Springer, 1929, p. 222.

entsprechen." (It is possible also that an old phylogenetic mechanism crops up here, to which correspond anatomic connections between the nuclei of the brain stem.) Kaminsky<sup>3</sup> has also published reports of two cases and has made a careful study of the mechanism involved.

#### REPORT OF CASES

**CASE 1.—History.**—W. F. C., a man, aged 27, who was referred by Dr. Angus McLean, had been healthy until his tenth year, when he fell from a swing, striking his head on the edge of a board. For several hours he was unconscious, and there were severe headache and vomiting for several days. On the day after the accident, it was noticed that the right side of the face was paralyzed. Convalescence was uneventful in other respects. He cannot recall whether the eye was excessively dry or not. About ten months after the injury, return of function was noticed in the right side of the face, and soon he was able to move all of the facial muscles. However, several new symptoms appeared coincidentally with his recovery; the right lid-slit grew smaller than the left; the right nasolabial fold became deeper than the left, and when he ate tears would brim over the right eye and run down the cheek. When he had no food in his mouth the right eye was neither unduly moist nor dry. The smell of food, however, might produce a mild effect. This symptom has persisted up to the present time, a period of sixteen years. The excessive lacrimation never fails to appear when he eats and never occurs under other circumstances. The patient is a traveling salesman and has been greatly embarrassed by his peculiarity, for people often stare at him when he dines in public.

**Examination.**—The patient was well developed and well nourished. The right side of the face showed more tone than the left. The right nasolabial fold was deeper than the left; the right lid-slit was smaller than the left, and the right eyebrow was higher than the left. When the patient wrinkled the forehead, the right side of the mouth was retracted and the right eyelid was partially closed; when he showed his teeth, the right eyelid was partially closed and the right side of the forehead wrinkled; when he closed his eyes, the right side of the mouth was retracted. In brief, he could not innervate any part of the right side of the face by itself. He invariably innervated the entire facial musculature. When salt or acid substances were placed on his tongue, moisture began to collect in the right eye after a latent period of a few seconds, and soon tears were running down his cheek. Any substance with a strong flavor produced the same effect, but no other procedure caused this reaction. Chewing and movements of the facial muscles were of no avail. The electrical reactions of the facial nerve were unchanged. Taste was preserved on both sides of the tongue. In other respects the cranial nerves were normal. There was no disturbance of motility or of sensibility. The reflexes were all in order. Medical examinations and laboratory tests, including the Wassermann test of the blood, gave negative results. Ophthalmoscopic examination revealed normal conditions. The lacrimal duct was probed, but no obstruction was found.

**CASE 2.—History.**—The patient, G. H., a man, aged 57, without apparent cause had a sudden violent pain in the left eye and left side of the head. He was not rendered unconscious but was dizzy and nauseated. He was put to bed at once

3. Kaminsky, S. D.: Ueber das Syndrom der Krokodils-Tränen, Deutsche Ztschr. f. Nervenhe. **110**:151, 1929.

but did not have medical attention. On the next day, he found that he could not close the left eyelid or move the left side of the mouth. However, he did not feel ill and was able to return to work. About three months after the onset, he was examined by a physician who found a complete left facial paralysis of peripheral type with a reaction of degeneration. The patient stated that the affected eye was always very dry. The blood pressure was 174 systolic and 98 diastolic, and the peripheral arteries were thickened. The Wassermann reaction of the blood was negative, and urinalysis revealed no sugar or albumin. About six months after the onset, there was some return of power in the left side of the face, and at the same time the patient noticed that the left eye would brim over with tears whenever he took foods into his mouth. Certain foods seemed to have more effect than others. For example, sour apples or hot soup produced more tears than other foods, but all types of food invariably caused more or less lacrimation. Appetizing odors had the same effect. There was never any weeping under other circumstances.

*Examination.*—Almost two years after the onset, the patient was well developed but somewhat undernourished. The left side of the face showed deepening of



Fig. 1.—Photographs of patient in case 2: *A* shows contracture of the facial muscles on the left side. *B* shows the teeth. The associated contraction of the left orbicularis oculi is evident. *C*, taken a few moments after the drinking of a cup of coffee, shows lacrimation of the left eye.

the nasolabial fold and narrowing of the palpebral fissure (fig. 1 *A*). It was impossible for him to move any part of the left side of the face without the extension of the innervation to all other portions of the facial musculature (fig. 1 *B*). There was no tendency to undue accumulation of moisture in the left eye until food or some other substance was placed in the mouth. Then the eye rapidly filled, and tears ran down over the left cheek (fig. 1 *C*). Voluntary movements of the face and chewing produced no effect, but mechanical stimulation of the inside of the mouth caused an overflow of tears. Taste was not affected. The other cranial nerves were normal. No disturbances of motility or sensibility and no alteration of the reflexes were detected. The blood pressure averaged around 160 systolic and 100 diastolic. The retinal arteries as well as the peripheral arteries were thickened, but the abdominal and thoracic viscera were healthy. There were a number of decayed teeth, several of which showed periapical abscesses. Evidences of mild hypertrophic arthritis were found in the fingers and spine. The Wassermann reaction of the blood was negative. The urine was normal.

CASE 3.—*History*.—M. S., an unmarried woman, 29 years old, had had bilateral interstitial keratitis at the age of 12 years. The Wassermann reaction of the blood was strongly positive, and she was treated by inunctions and by intravenous injections of arsphenamine. After several years of treatment, the Wassermann test became negative. On July 17, 1931, complete paralysis of the right side of the face developed over night. The patient could not close the eyelid, and the cheek sagged on the affected side. There was, however, no overflow of tears, taste was lost on the right side of the tongue. Approximately five months after the palsy developed, there was some return of power, and the patient noted that whenever she took food into the mouth or smelled an appetizing odor tears would overflow from the right eye. This never occurred under other circumstances and always occurred when she ate, although it was sometimes more marked than at other times.



Fig. 2.—Photograph of patient in case 3, showing lacrimation resulting from eating an apple. The contracture of the right side of the face is well shown.

The family history confirmed the diagnosis of congenital syphilis, for the father died while "insane" and the mother had several miscarriages.

*Examination*.—The patient was small and somewhat overnourished. Both corneas were cloudy, and the pupils were unequal, irregular and inactive to light. The other cranial nerves were normal, except for the right seventh nerve. At rest there was increased tonus on the affected side, shown by deepening of the nasolabial fold and narrowing of the palpebral fissure. Voluntary and emotional movements of the right side of the face resulted in contraction of all facial muscles, as described in the two preceding cases. It was clear, therefore, that misdirection of the regenerating motor fibers had occurred. When the patient took any food into her mouth the right eye soon began to brim over with tears (fig. 2). During the examination the patient became despondent and wept several times. It was observed that lacrimation was about equal in the two eyes. The right facial muscles reacted well to faradic and galvanic stimuli, although a slightly stronger current was required on the right than on the left. Neurologic examination gave

negative results in other respects. Medical examination showed no evidences of visceral disease. The Wassermann reactions of the blood and spinal fluid were negative.

*CASE 4.—History.*—The patient, J. B., a man, aged 70, began to suffer from violent paroxysms of vertigo and vomiting in July, 1930. The symptoms grew worse during the next year, but none of the physicians whom he consulted could give him any relief. In April, 1931, he consulted Dr. Dandy, who discovered that he was partially deaf in the left ear and made a diagnosis of Ménière's syndrome. Examination at that time revealed no abnormalities, except about 70 per cent loss of hearing in the left ear, affecting chiefly the high notes. A few days later, the left eighth nerve was sectioned in the posterior fossa. The attempt was made to avulse the nerve, but it was so firmly adherent to the seventh nerve that it was found necessary to cut it. However, the seventh nerve must have been injured, for several days after the operation it was noted that the left side of the face was paralyzed. The eye was dry and soon became much inflamed, although sensibility was intact. For a time it was necessary to keep the eye closed by a pad. The vertigo was abolished at once, and the patient has enjoyed complete freedom from the original symptoms since the operation. After several months (the patient thinks about five months) power began to return in the left side of the face. At the same time he noted that whenever he took food into his mouth tears would run over the left lower eyelid and course down the cheek. He did not notice this under other conditions. This symptom became so annoying that he stopped eating solid food as far as possible, for he found that if he gulped liquids down very quickly his eye would remain dry. The odor of food did not cause lacrimation, perhaps because the patient had a poor appetite and the smell of food aroused no desire to eat. In July, 1932, the patient came to Baltimore to consult Dr. Dandy about the lacrimation and was referred to me for neurologic examination.

*Examination.*—The patient was in excellent general condition and seemed to be much younger than his given age. Neurologic examination revealed complete deafness in the left ear as a result of the operation. The left lid-slit was smaller than the right, and the left nasolabial fold deeper than the right. It was impossible for the patient to move any part of the left side of the face without at the same time innervating the entire facial musculature. The sense of taste was preserved, and the facial muscles responded to faradism. Stimulation of the tongue with salt or acids caused increased lacrimation in the left eye.

#### ANATOMY AND PHYSIOLOGY OF THE FACIAL NERVE

The seventh nerve is composed of several portions: a motor component formed by axons of cells lying in the pons and supplying the superficial musculature of the face; a sensory component arising in cells of the geniculate ganglion and conveying gustatory impulses from the anterior two thirds of the tongue and perhaps deep sensibility from the face, and an automatic component which furnishes secretory and vasodilator fibers to the submaxillary and sublingual glands. Several authorities<sup>4</sup> have stated that the facial nerve also supplies secretory

4. Müller, L. R.: *Die Lebensnerven*, Berlin, Julius Springer, 1924, p. 127.

fibers to the lacrimal gland. Poirier and Charpy<sup>5</sup> claimed that these fibers arise from small cells adjacent to the facial nucleus and form a part of the nervus intermedius until the geniculate ganglion is reached. There the secretory fibers enter the great superficial petrosal nerve which makes its exit from the facial canal through the hiatus fallopii, and passes forward in the middle cranial fossa to the outer side of the internal carotid artery, where it is joined by the great deep petrosal nerve and becomes the vidian nerve. The latter then enters the vidian canal and joins the sphenopalatine ganglion. Here the preganglionic fibers end in relation to the postganglionic neurons which, in turn, send their axons

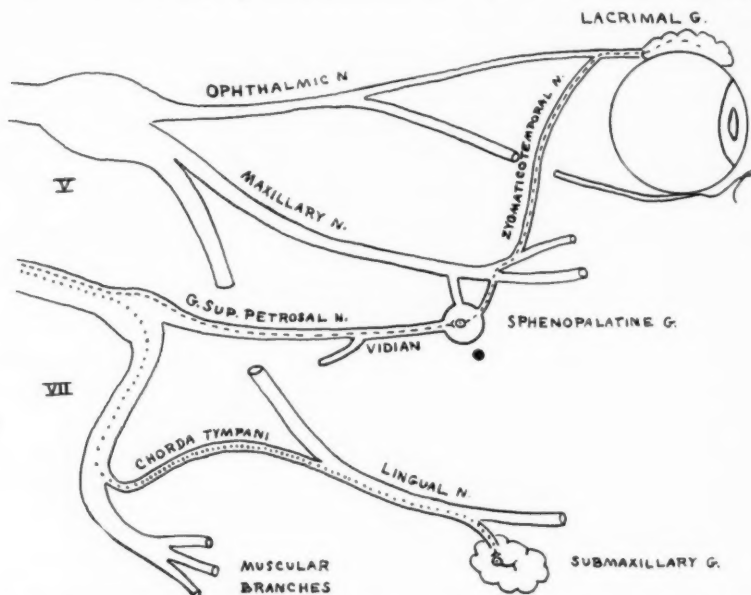


Fig. 3.—Diagram showing the pathway of the secretory fibers supplying the lacrimal gland and the salivary glands.

by way of the sphenopalatine nerves to the second or maxillary branch of the fifth nerve, a branch of which unites with the lacrimal branch of the first division of the fifth nerve, which finally conveys the secretory fibers to the gland. These relations are shown in figure 3. Clinical and experimental observations seem to support these statements strongly. It is well known that section of the fifth nerve by the temporal route, in cases of trigeminal neuralgia, frequently results in loss of lacrimal secretion. Dandy<sup>6</sup> has shown that this is due to injury of the great

5. Poirier, P., and Charpy, A.: *Le système nerveux*, in *Traité d'anatomie humaine*, Paris, Masson & Cie., 1901, vol. 3, p. 856.

6. Dandy, W. E.: An Operation for the Cure of Tic Douloureux: Partial Section of the Sensory Root of the Pons, *Arch. Surg.* **18**:687 (Feb.) 1929.

superficial petrosal nerve which occurs when the dura is stripped from the base of the skull; for when the posterior route is chosen and this nerve is not affected there is no diminution of tears. He has also reported a case in which the seventh nerve was destroyed in the posterior fossa with complete cessation of tear secretion. Lutz<sup>7</sup> cited cases in which destruction of the sphenopalatine ganglion, the great superficial nerve or the geniculate ganglion resulted in loss of tear secretion. Reflex lacrimation, of course, is lost when the cornea and conjunctiva are rendered anesthetic by lesions of the fifth nerve in any part of its course. Sympathetic fibers also reach the lacrimal gland, but it is well known that section of the cervical sympathetic nerve does not affect lacrimation.

## COMMENT

*Theoretical Interpretation.*—It is necessary first to discuss the cause of the so-called facial contracture which commonly follows severe facial palsy of the peripheral type, for there is reason to believe that this symptom is intimately associated with paroxysmal lacrimation. By contracture is meant a state of increased tonus on the affected side of the face. Careful examination of a patient so affected will reveal the following facts: The contracture is not always present to the same degree. It is more obvious when the patient is active and animated and inconspicuous or absent when the patient is relaxed. It is always found in connection with abnormal associated movements of the face. Thus, when the patient closes the eyes, the corner of the mouth on the affected side will be retracted and the nasolabial fold will grow deeper. In other words, the contracture is accentuated. When the patient smiles or shows the teeth, the eyelid is partially closed. Even the minimal innervation concerned in spontaneous winking will usually produce a slight twitch of the corner of the mouth. It is thus evident that impulses which were formerly directed to an isolated group of muscles are now diffusely distributed throughout the entire facial musculature, and it is impossible to innervate any part of the face without at the same time innervating all other parts. The only logical explanation is that advanced by Spiller<sup>8</sup> and others, namely, that the regenerating nerve fibers have become misdirected so that they no longer reach the muscles which they formerly supplied, but are scattered at random over the face. The bundle of fibers which innervated the orbicularis oculi, for example, before the facial palsy developed is distributed among all the facial

7. Lutz, A.: Ueber die nervösen Bahnen der Tränenabsonderung und deren Störungen, Arch. f. Ophth. **126**:304, 1931.

8. Spiller, W. G.: Contracture Occurring in Partial Recovery from Paralysis of the Facial Nerve and Other Nerves, Arch. Neurol. & Psychiat. **1**:564 (May) 1919.

muscles during regeneration, and hence nerve impulses flowing along these fibers will cause a diffuse reaction. As a result, all nerve impulses that play on the facial muscles, whether they are the result of emotional, voluntary or reflex reactions, are distributed over the entire face. Each muscle, therefore, receives as many impulses as all the facial muscles together receive under normal conditions, and, as a result, muscle tone is increased. Several facts support this hypothesis. The phenomena appear coincidentally with the return of function and only when the nerve has undergone degeneration. They are never seen following the mild and transient facial palsies in which the electrical reactions of the nerve remain normal. The contracture is not the result of an irritative process, for it will persist for many years without modification. It is not due to fibrous shortening of the facial muscles, for it will disappear partially or completely when the patient is relaxed. Some of the sensory disturbances which follow the regeneration of cutaneous nerves may be simply explained on the same basis.

I have stated in the preceding section that the facial nerve contains several groups of fibers, not only motor fibers destined for the facial muscles, but secretory fibers for the salivary and lacrimal glands. I have shown, furthermore, that the motor fibers may become misdirected during regeneration of the nerve and may finally innervate muscles other than those they originally innervated. In one of my cases, electrical tests revealed reactions of degeneration several weeks after the paralysis appeared. In the other cases it is probable that the nerve underwent degeneration, for the paralysis persisted for a number of months. In all instances contracture and abnormal associated movements of the face appeared during the stage of recovery, so that one may conclude that the motor fibers at least were misdirected during regeneration. Paroxysmal lacrimation developed at the same time as the contracture, and has persisted in one case for sixteen years and in another for nearly two years. It always occurs when the patient is eating or when substances with strong flavors are placed in the mouth. The patients, therefore, lacrimate whenever they salivate. I suggest that some of the secretory fibers which formerly supplied the salivary glands have become misdirected during regeneration and have formed connections with the lacrimal gland. It is of great interest that the patients could not provoke lacrimation by voluntary movements of the facial muscles. Apparently, therefore, motor fibers of the facial nerve either did not reach the lacrimal gland or, if they did, were incapable of exciting secretion.

The reader may well ask why paroxysmal lacrimation is not seen more frequently, since facial palsies are common. Perhaps lacrimation occurs in many cases but does not attract attention, for it is confused with the overflow of tears that is so common in the earlier stages of

the palsy. However, it seems probable that the lesions in the cases described here were in an unusual site, i. e., proximal to the geniculate ganglion. In case 2 the onset was very sudden, almost apopleptic. The patient was an elderly man suffering from arteriosclerosis and hypertension. It is likely that a vascular lesion occurred, involving the nerve in the proximal part of the facial canal. In case 1, the palsy was the result of a severe trauma, which probably fractured the skull and may well have injured the nerve in any part of the canal. In case 3, the patient had congenital syphilis. Case 4 was the most instructive of all, for the lesion was undoubtedly in the posterior fossa and

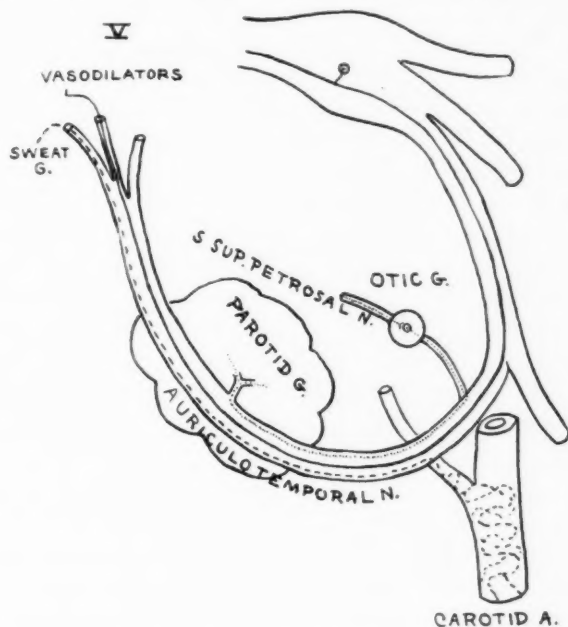


Fig. 4.—Diagram showing the anatomic relations of the auriculotemporal nerve: The secretory fibers of the parotid gland are shown by the dotted line, those of the sweat gland by the broken line, and the vasodilator fibers by the solid line.

therefore proximal to the geniculate ganglion. It is of interest that the patient's eye was dry for several weeks after the operation. In each case, therefore, the picture was quite unlike that of the common Bell's palsy which probably involves the nerve more distally.

*The Auriculotemporal Syndrome.*<sup>9</sup>—This strange condition may be discussed at this point because it seems to present many analogies to the

9. Fridberg, D.: Das auriculo-temporal Syndrom, Deutsche Ztschr. f. Nervenhe. 121:225, 1931.

paroxysmal lacrimation described. It is a sequel of penetrating wounds, suppuration and surgical incisions in the region of the parotid gland which sever the auriculotemporal branch of the third division of the trigeminal nerve. As a result, an area of anesthesia may be found over the temple. If the nerve regenerates, a very interesting group of symptoms may appear. Whenever the patient eats or takes food into the mouth, the area which was formerly anesthetic becomes bright red and is covered with droplets of sweat which run down over the cheek. That is to say, paroxysmal sweating and vasodilatation appear over the distribution of the auriculotemporal nerve when the patient salivates. At other times this region is indistinguishable from areas of normal skin. These phenomena constitute the auriculotemporal syndrome. The simplest and most logical explanation for these symptoms is analogous to that offered for the paroxysmal lacrimation. The auriculotemporal nerve contains afferent fibers conveying sensory impulses from the skin, vasodilator fibers destined for the subcutaneous arterioles and secretory fibers for the sweat glands which are derived from the cervical sympathetic system. For a short distance near the parotid gland the nerve is accompanied by secretory and vasodilator fibers which supply the parotid gland and are derived from the ninth nerve by way of the otic ganglion. These relations are made clear in the accompanying illustration (fig. 4). It is evident, therefore, that when the nerve is injured between the parotid gland and the point at which it receives its communication from the ninth nerve the various groups of nerve fibers enumerated may be severed and, in the process of regeneration, may become misdirected along pathways other than those they originally pursued. It seems probable that the auriculotemporal syndrome is the result of the misdirection of some of the secretory fibers of the parotid gland so that they form connections with the sweat glands and blood vessels of the skin. As a result, when the patient is eating and a volley of nervous impulses passes over the parotid fibers, paroxysmal sweating and vasodilatation occur in the distribution of the auriculotemporal nerve.

## NONORGANIZATION AND DISORGANIZATION OF THE PERSONALITY DURING PSYCHOSES

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BALTIMORE

In recent years psychiatry has recognized the importance of a study of the personality and has tried to determine its share in the psychotic reaction from the point of view of personality reactions. By personality I mean the psychobiologically integrated unit which has developed and is developing during life. One can see an increasing organization of the personality from infancy to maturity, but not all personalities reach full organization, and in many people certain aspects of the personality are less organized or integrated. In the feeble-minded group there is primarily a lack of organization of the intellectual aspect. In other types of psychopathic make-up, other parts of the personality may be less developed and organized. Physical and mental development in the broadest sense are not parallel. It is also known that some organs of the body develop sooner than others. One speaks of maturity, therefore, when the whole personality has reached a degree of organization which harmonizes the various strivings with integration of emotional and intellectual resources, utilizing the experiences of the past and adjusting imagination and anticipation to reality.

In this discussion I intend to limit my observations to immaturity and shall not include psychopathic personalities and motor nonorganization such as may lead to torticollis and stuttering. I also shall not discuss the lack of integration of the sexual domains, which sometimes lead to certain maladjustments and perversion problems.

In the development of the personality one is able to distinguish various phases, and it is known that only a limited degree of organization can be expected during the phase of infancy, early childhood, puberty and late puberty or adolescence.

In the mature person the various strivings of the personality are brought to a harmonious unit. Contradictory strivings are more or less adjusted to one another. This leads to consistency and unity of the personality in experiencing and acting. In order to achieve this, a personality cannot be too loose; it must have a certain degree of organization. On the other hand, too rigid an organization is a handicap, leading to exaggeration of certain features and to inability to make adaptation. From childhood to maturity the human personality develops from a loose to a plastic but well organized unit. Marked ambivalency (i. e., more or less automatic or at least unpredictable emotional or other kinds

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of swings), which is still present in the adolescent, is excluded in the mature person. After the age of maturity has been reached, few fundamental changes in the personality can be expected. Certain features and tendencies may become more marked, adjustment to life may influence interests and strivings, but no essentially new characteristics appear. In later life the personality loses its plasticity and various features become more marked and crystallized.

One has to consider the right of autistic thinking and the right of privacy in every personality, but one expects the mature imagination to be willing to be tested with reality, or at least that the mature person realize what is to be kept apart as imagination. The formative influence of life experiences, at the time of occurrence as well as later, has to be stressed, but one should not make formative factors the exclusively important factors and neglect to stress the constitutional material.

In schizophrenic reactions there is a disorganization of the personality, and particular strivings and features which one is accustomed to see only in the nonorganized personality come again to the foreground. On the other hand, a nonorganized personality will show similar features in an affective psychosis.

In affective psychoses in immature personalities one notices rather characteristic features which are the same as in the affective psychoses of adolescence. The case of a boy, aged 14, who was seen in three attacks, may illustrate the change which is due to increasing maturity.

CASE 1.—In the first manic excitement, which started after the boy had been frightened by a joke indicating criminal prosecution, he became confused and made mistakes in work. He was restless, called his parents strangers and was afraid that they were going to do away with him. At the same time he was cheerful, whistled, and continually addressed strangers on the street; he was over-active and wanted to fight other boys. This condition changed several times a day to brief states of irritability and sulkiness. He always described his mood as fine, and showed marked distractibility, flight of ideas and a great deal of play acting. The physician was mistaken for a friend. He also remarked that everything was changed—stores, automobiles and buildings seemed larger. He said that he was not scared but did not want to be alone in the room at night because "some one was under the bed," and he "heard and saw things." Noticing the radiator holes in the wall, he believed that dictaphones were in the room. He felt electricity in the bed and in the atmosphere, and looked behind him because he thought that somebody was there to untie his nightshirt (besides these sexual indications there were frank sexual desires and masturbation). He heard voices saying "Bah," or "Somebody got my keys." Besides elation, irritability, sulkiness and fright were the outstanding features of mood disturbance. After twelve days he became slightly depressed, which was expressed by feeling "homesick" and "lonely." After about two more weeks he recovered completely.

This patient was a cheerful, excitable, socially well liked person, who was very sensitive to teasing, especially about his small size. From 12 to 13 he had masturbated, but not again until a month before the onset of the illness.

Three years later (at 17) he returned. For three or four weeks he had been restless; he was more sensitive when he was rushed by work, complaining of not feeling well because of a cold. The day before admission he cried and felt that the men in the office were "kidding" him; he became excited, overactive and restless, constantly laughing and whistling, but easily changing to spontaneous crying. Again the building seemed larger and he mistook people in the ward of the clinic for friends (misidentification on the basis of familiarity). In the clinic he again showed elation, overtalkativeness, flight of ideas and distractibility, changing quickly to crying and irritability. He heard indistinct voices ("echo-like"), and felt that people were talking about him. At night he was apprehensive again, because of the "fear of being alone," and held the nurse's hand. All the time he felt that a joke was being played on him, and he felt unnatural. He was preoccupied with having been too much with girls and with consciousness of his short size. He felt confused and talked in a fearful way of seeing his father (probably misidentification and not visions). Afterward, he had a "hazy memory" of this episode. When he saw torn-down buildings he believed this was due to an earthquake. He often thought that everybody was afraid of him, and reassured the nurses. Many times he was sarcastic; then again he sang, whistled and was pleasant. There were daily changes to apprehension, weeping and anxiousness, and he always expressed marked sympathy for the suffering of other patients. After nine days he changed, becoming "homesick" and "blue," and again seemed to recover after a stay in the hospital of two weeks.

The factors that played a rôle in this second illness were sensitiveness to teasing and jokes played on him, to his size and to worries about his first petting experiences. He was proud but lacked confidence in himself, which was expressed by shyness with older people.

Ten days after discharge (this second illness had lasted six weeks) the patient again became sleepless and overactive; he sang, spent money freely and sometimes wept and was sarcastic. This third illness lasted eleven days. He now had become frankly manic; he showed irritability, combativeness, overtalkativeness, flight and an attitude of bravado, manifesting pure self-assertion without any features of confusion, fear, unreality or voices. The content at times was grandiose; at other times he was swearing and impudent. There was no crying, except when he changed to a slight depression, which again he was unwilling to admit and described as homesickness. In addition to the previously mentioned factors, he described a difficulty of adjustment to his father's death (three years before), resentment about too much mothering and difficulties of sexual adjustment.

This patient has since made a good adjustment. He is an active, cheerful, sociable, independent person, happily married and working steadily in an office. At 25 he had a depression which lasted about three months. During this psychosis there were no unusual features and no marked disorders in thinking, impure affects or homesickness.

The unusual features in the first, and to some extent in the second, manic excitement are characteristic of adolescent excitements. They can be explained by similar features in normal adolescents. In adolescents there is not only an intellectual development but also an increasing organization of the whole personality. The adolescent becomes aware of himself and his independence, as well as his further relations to the environment. He begins to take the future much more into account and tries to plan, but he has also far-reaching imagination which has

not yet been tested with reality. On account of this development, he begins to think about his problems, to feel isolated from others—frequently expressed by loneliness—and gropes for a solution of his difficulties. Occurrences are easily related to himself. He is sensitive but in the earlier years of adolescence frequently hurts other people's feelings by tactless remarks. In some cases a development of sympathy and a desire to help others are more pronounced. The imagination is still egocentric, but there are more longing and a desire to reach beyond the present status. At this time feelings of inadequacy therefore develop easily. The adolescent child begins to become emancipated from his old environment and old influences and beliefs. Some speak of a negative phase of adolescence characterized by restlessness, opposition to family and society, increased sensitiveness and therefore irritability and frequently a feeling of loneliness and inadequacy. Later this phase develops in a more positive direction, when the adolescent begins to have a sense of the evaluation of beauty, ethics and social possibilities, but even at this time he still is torn between different desires and strivings. Further development leads to an increasing self-reliance and to an adjustment of contradictory strivings into a more uniform and harmonious picture. The original isolation changes to fitting into society without losing one's own individuality. At this stage the adolescent begins to be creative and constructive in his thinking. He is able to find his way in religious and philosophic problems and to adjust himself to society. His imagination gradually begins to deal more with possibilities, although vague longings may still be leading. The religion of fear is gradually oriented along an ethical line. In many there is a dropping out of religious needs or a breaking with tradition by the building of a new religion. This religious development may be accompanied by conversion and estatic experiences. Mystical tendencies may or may not be connected with sexual development. The problems of death and eternity, of God and creation, of soul and matter are frequently perplexing. Their solutions are usually not productive, but merely expressions of longings and needs. Thinking becomes more abstract and discriminative, and conclusions by analogy are avoided. There is frequently a marked development of self-analysis or of analysis of others. Imagination may have much to do with romantic ideas and hero worship. In daily life this may be seen in the enthusiastic allegiance to some teacher or older friend or in "crushes." This does not necessarily need to be on a homosexual basis. There is still a marked tendency toward identification with others, but this diminishes with gradually increasing individualization. The world begins to seem more real and its perplexing problems clearer, but, naturally, in such a period the feeling that things are unreal can easily occur under stress.

The motility development is usually parallel with the gradual organization of the whole personality. In early adolescence there is a tendency to grimacing, awkward movements or gestures and expressions of embarrassment—characterized by loud talking, embarrassed whistling or gestures, impulsiveness and the pleasure in purely physical activity which is so characteristic of childhood. The degree of these manifestations differs according to the personality involved. With progressing maturity the motility becomes more integrated.

The sexual development has probably been studied more closely than the other aspects. In puberty there is much repetition of previous strivings; anal-erotic, sadistic, homosexual, heterosexual and also narcissistic tendencies appear and frequently create insoluble problems. The desire for affection, characteristic of childhood, is now combined with the possibility of offering love and physical gratification to others. The strivings of physical desires and love become gradually united.

In the case cited there are many features which one can understand from studying normal adolescents. I stress here the patient's desire to fight with other boys, his play-acting and use of fantastic elaborations, his expression of depression by the feeling of homesickness—which indicates lack of emancipation—and his easy change in emotions; so that there are, besides manic or hypomanic features, fear, slight depression and particularly stubbornness and sulkiness. The latter features are reactions of defense to situations that are not sufficiently intelligible and, therefore, cannot be mastered, but to which the person is unwilling to submit and adjust himself. In behavior, in many cases, there is a marked ease in contact with others; in addressing strangers, often impudence or teasing. Such patients are overactive and playful and often act a part—with much grimacing, decorating of themselves, whistling and singing. On the other hand, in this case, there was a tendency to unreality feelings and to identification with others or a tendency to identify others with people the lad knew. This was accompanied by definite confusion in thinking. His memory for the illness was hazy, probably because of confusion in thinking. In the hypomanic state especially he showed mischievous behavior and reaction, with remorse and crying or sulky and sullen behavior when reprimanded. There were frequently noticed marked appetite and stealing of food, and occasionally lying and stealing. The inability to stick to promises of an ethical kind is often most distressing. Many patients are erotically excited; others pray much and have religious preoccupations. In slight depressions there are complaints of homesickness, sobbing for the parents and marked sensitiveness, but also sympathy for others and inadequacy feelings, frequently mixed with temper tantrums and sulky and irritable behavior. Many patients are unable to discuss

their illness, and sit around looking sullen and often stuporous. This condition, however, clears up rather rapidly. Spite and jealousy, an attitude of opposition to others, a tendency to imitate others and ridicule them and resentment, together with a great desire for affection and need of being affectionate toward others, are sometimes found in slight depressions but are more frequently found in hypomanic states. Insecurity (i. e., as yet insufficient dependence on self) is indicated by apprehension and fear, and is seen in both depressions and hypomanic reactions.

The adolescent preoccupation with family relationship is often expressed in the idea of being an adopted child. Body curiosity leads to fantastic sexual and anatomic theories, with pondering about left and right and symmetry. There is a marked tendency to visual hallucinations at night, especially those of a fearful type, and auditory hallucinations with content in accordance with the dominant mood and preoccupations. Sensations of electricity may indicate sexual feelings.

As I have stressed before, the development of the personality is frequently delayed. One must realize that some people do not begin to mature until they are in the twenties. Others never reach complete organization. To the latter group belong persons whom we usually call immature. Features of immaturity in the adult are: lack of control of emotional display (easily thrilled and enthusiastic, but also easily discouraged and frequently making thoughtless criticisms), need for affection (which is not always connected with real sympathy for others but rather with cruelty), antagonism toward some people and their ideas and sympathy toward others and their ideas. This is especially marked in religion. A constant craving for something new and a desire for change, a liking for romantic stories and adventures, a tendency to brag and to make up stories with the desire to be the hero, revolt against things as they are, and superficial cynicism and an interest in children's play and in being with children are frequently observed. Their emancipation is insufficient. They are dependent on others, especially on parents or, later, on husband or wife, the minister or domineering friends, and feel homesick when they are away from home. They are resentful to criticism and react with sulky and surly behavior. There is a tendency to be revengeful and a desire for retaliation. In many there are a marked fear of the dark and childish fears of robbers. (Such fears are not necessarily on a sexual basis but can be due to immaturity in imagination and habit formation.) Occasionally, immature thinking is characterized by lack of constructive discrimination. (This, in the setting of a depression which causes disorder in thinking may easily lead to confusion, with feelings of unreality and unfamiliar-

ity or its opposite.) On the whole, there is a lack of consistent activity and of expression of genuine individuality.

Occasionally the immaturity accompanies physical immaturity, and one then speaks of "infantilism" and "puerilism." This group has been studied, but probably not sufficiently with regard to the psychotic reactions. In this group, as well as in some acromegalic disturbances, one finds affective and paranoid psychoses which present a picture similar to the adolescent affective psychoses. Many of Kleist's "confusional psychoses" no doubt belong to this group.

One also frequently finds not fully organized, immature personalities in patients who react easily with fear and panics. It is probable that what one calls neuropathic personalities in children and in adolescents often belong to this group.

One can easily see that immaturity may be responsible for features in affective psychoses which resemble schizophrenic symptoms, but such features have to be evaluated differently according to whether they are the expression of nonorganization or the expression of a disorganization which has led to the appearance of abnormalities.

CASE 2.—A college student, aged 19, who had not matured according to his age, was still dependent on his mother and, although sociable, felt ill at ease with people because he lacked confidence in himself. He had suffered from enuresis until the age of 7, and until a few years previous to admission had slept frequently with his mother when he was worried. He was very sentimental. For the last two years he had been infatuated with and dependent on an older woman, who took a motherly interest in him and kissed him occasionally. When he had to take a job because of financial difficulties, he reacted with slight depression and marked seclusion. He thought that people were looking at him, felt ill at ease and was afraid of insanity. His main complaints were confusion and dizziness. The depressive features were not marked; they were mostly expressed by hypochondriac concern (clicking in the ears, weakness in the knees, dizziness and feeling as if he were walking on air), homesickness and demanding to be with the woman with whom he was infatuated. He wanted to commit suicide but lost his nerve, and shot himself through the toe to indicate his disgust with life. His depression and complaints cleared up suddenly after about two weeks. This was followed by a mischievous phase, in which he was impulsive, boisterous and impudent, stole little things and played tricks on other patients. He was always penitent when brought to task. He often seemed drowsy, and wanted to sleep a great deal. After discharge from the hospital, he entered the army while still slightly hypomanic. He had by that time developed more frank elation; he said that he was "feeling just fine," and was overactive. After about six months this was followed by depression for three months, in which he was suspicious, feeling that people were watching him; that his mind was being tested because he was a spy, and that his superiors wanted to try to prove that he did not properly perform his duty. He cried easily and also laughed frequently. Usually he was apprehensive; during the interview with the physician, he feared that somebody was listening in. He could not understand why he was constantly spied on. With the clearing up of the depression he began to feel at ease, and all the other symptoms disappeared. He was well for seven years (protected by college life and

postgraduate work), but again a depression developed when he had his first position as a high school teacher. This depression (at 27) was characterized by a frank depressive mood with daily variation, difficulties in concentration and a slight fear of insanity. He was unable to associate with other patients. Any mention of home increased the depression and caused tears. He finally left the hospital too early because he was homesick for his wife. All the time he needed a great deal of sympathy and played for it. After a few weeks at home he was able to make a good adjustment and has been successful (present age, 33).

This patient is still immature in many ways. He has never become emancipated from his mother and is now also greatly dependent on his wife. The depression was caused, no doubt, not only by his feeling of inability to carry on his work (owing to his lack of self-confidence) but by the fact that his wife and mother could not get along together and he was unable to decide in the matter. He had chosen an inferior position in order to be near his mother. His sensitiveness is still marked, and he shows it more easily than a mature adult would. Even when well he has a marked need for sympathy and plays for it. He gets along well with others and is eager to please, but is also argumentative. He is very affectionate and sentimental, and is devoted to his wife. At the same time, he is not greatly worried about an experience in extramarital intercourse. He is not thoughtful of his wife; when his feelings are hurt, he is often sulky, and sometimes speaks of separation. In planning and decision he is indecisive, frequently indulging in day dreams without trying them out in reality. He is usually cheerful and apparently full of confidence. He becomes easily dissatisfied with his work, however, although he is always enthusiastic when he starts out, and he would like to take a degree along another line. Sexually he is insufficient, suffering from premature discharge, but he wants frequent relations. His feelings of inadequacy are exaggerated by his marked conscientiousness in his work. The physical make-up is characteristic. He is slender, with feminine distribution of hair, representing a mild hypogenital state.

In this case one can see that there is an increase of maturity over that in the last depression; immaturity, however, is still characteristic of his poorly organized personality. One no longer finds the feelings of uneasiness and suspiciousness, and since the last illness he has developed even more stability.

An entirely different dynamic development is present in the next case, that of a student, aged 21, in whom I was able to follow the increasing organization of personality from childhood through puberty and to observe the results of disorganization at the beginning of the twenties.

CASE 3.—The patient was a sexually precocious boy (from 2½ to 10 years of age he had had scattered sexual experiences; from 10 to 13 years of age he was sexually aggressive, talking to prostitutes, going to petting parties with older teachers and watching them during classes). He had been a difficult child; he was stubborn, with lack of control of his quick temper and reacting frequently with temper tantrums; he was shy but friendly with other children, and very sensitive to criticism. The period I am discussing is from 5 to 12—the onset of puberty. During this period there were frequent stealing, cheating at school to better his marks and lying, partly due to his wealth of imagination and partly to

avoid punishment or to gain appreciation by boasting. There was an increasing need of appreciation, and he therefore played the roughneck, although he was afraid of fighting and of punishment. In school and at home he was mischievous and showed a great talent for mimicking people. He liked to tease others but was very sensitive to teasing; he was sulky and revengeful, and cried easily. There was a great need for affection, but he did not show it. Since 6 he had been devoted to his mother and had developed increasing hate for his father and, to a less extent, for a more successful brother. At school he was inattentive and did poorly. He was therefore considered feeble-minded by his parents and was constantly told of it. When called on to recite, he was tense and self-conscious. He belonged to the orthodox Jewish group and was active in church activities. At 10 he began to play the violin, but stopped it at 16 because of lack of recognition in his orchestra.

At 12 he had the first erection and at 13 the first emission. From 12 to 14 there was a period of masturbation. Emissions were accompanied by dreams of intercourse with his mother and dreams in which boys (for instance, his brother) and girls appeared. At 13, when transferred from a socially inferior to a better neighborhood and to a city high school, where scholastic achievements and not rough behavior were highly estimated, he began to change. He developed a desire to do well and to be a scholastic leader. His shyness made social adjustment impossible and did not satisfy his desire for companionship. During the high school period he became increasingly self-conscious and tense. He lost interest to some extent in his personal appearance. He developed a strict ethical code, did not lie or steal, but still cheated occasionally in order to better his scholastic standing. This apparently did not interfere with his marked conscientiousness. Due to social maladjustment, he felt lonely, especially as he was unable to participate in athletics because of asthma. He developed definite sexual control and stopped the habit of watching girls. He believed that owing to this hard work for scholastic standing he was not bothered by sexual desires. He was imaginative, but he recognized his lack of originality and made futile attempts at correction. Previously he had merely imitated people. He was cheerful but often gloomy, affectionate, sympathetic to others, emotionally easily moved, impulsive and quick-tempered, with a lack of self-restraint. He still felt resentment when given poor marks at school, but made no attempt at correction. He usually had an attitude of aggressive self-defense toward the teachers and toward authority, which he gradually began to overcome at 17. Owing to his appreciation of his own scholastic success, he began to look down on his uneducated father and became closer to his brother. His ideals were students who were scholastically and socially successful. When confronted with a task, he was greatly afraid of failure. His thinking became more constructive, and he developed definite planning and concreteness. He was good in languages and where imagination entered, but poor in mathematics and in laboratory work. Until the late years of high school he was afraid of and antagonistic toward leading and commanding personalities. Then he began to admire them and to attempt to reach their level. He was less mischievous, only occasionally mimicking people, but still very sensitive to ridicule and teasing. There was less day dreaming. Occasionally, when somebody hurt his feelings, he was sullen and revengeful. (Some of the sluggishness which he attributed to asthma was probably day dreaming.) The content of his imagination was that of his age—resulting from hero worship and the reading of romantic and adventurous stories. He showed religious emancipation at around 13 by turning away from religion, but he still went to the synagogue. Previously he

had studied Hebrew and was awed by God. At 18 he began to broaden out into philosophy and to become increasingly self-dependent.

When his illness started (at 20), in his second year at a university away from home, he was studying philosophy with the determination to understand it, although he had great difficulty. He was especially interested in Spinoza and in Hebrew, because he had become aware of racial antagonism in his environment. (Although that antagonism must have existed in his high school environment, where he was the only Jew, he was not aware of it.) From his study of philosophy he wanted to get power and an understanding of God. In social matters he worked hard to achieve leadership. He also wanted to be a scholastic leader and was resentful of poor marks. His goal was to become a great scientist. He was unable to see the justification for his poor marks, as he had worked so hard. Sexual strivings came again to the foreground. There were some transient imaginations of becoming sexually very powerful (having read Rabelais), and mere admiration for a woman student changed to an autistic love affair. Physical sexual desires were never dominant. This increasing attempt at finding himself met with failure, which led to disorganization.

Instead of giving a detailed account of the development of the psychosis, I shall attempt to point out the various features of the disorganization and their relation to previous personality features. I might add briefly that the patient developed rapidly an acute picture of hallucinosis with mystical experiences and vague paranoid influence, some odd behavior and transient motility involvement. After about two weeks the illness developed into a subacute stage with occasional exacerbations of a smiliar type, and great improvement after about a year.

The interesting features of disorganization that were noticed in this patient were: mystical experiences along a religious line, feeling in contact with God, accepting messages from Him in the way of impulses and voices which forced him to carry out odd activities (passivity reaction). It was a revolt against God with submission, a marked fear of God such as he had experienced at 13, when he had gone through an experience of feeling scared by silence and eternity. The problem of eternity again came to the foreground, and the patient began to think in terms of billions and trillions of years. The Jewish racial problem became dominant. Suddenly he felt ostracized and wanted to associate only with people of his own race, turning to a rabbi for first help, but having at the same time a great desire to associate with the Gentile group of high school days. There was a mixture of shame and pride in being a Jew. His sexual desires were greatly stirred up. The idealized infatuation of the autistic type turned to an autistic intercourse experience, in which he felt purified by having intercourse with that girl. Masturbation, which had ceased at puberty, again became important. Intercourse (in masturbation experience) meant intercourse with God. He felt that he was able to have intercourse with that girl by breathing. He believed that he would be able to change into a woman, which was the destiny of man, and tried to put his penis in his mouth, thus trying to impregnate himself. He felt that women were constantly changing into men, and that he then would have to go to Mars. Similar conceptions are found occasionally in the adolescent sex upheaval, and one finds them also in mythology and in the customs of primitive people. He had intercourse with nature and with trees, and experienced ecstasy, the mystical union with the universe. He again felt scared when he heard silence. Anal-erotic tendencies became marked. He had to wash his face in water from the toilet and to smear, in order to punish himself, as well as for sexual pleasure (as a child, defecation had been very disgusting to him). Homosexual dreams

again came to the foreground. His emancipation problem was very important, characterized by increasing hate toward his father; he felt at the same time sexual stimulation when close to him, and devotion to his mother. The sexual tension was noticed in sensations in the soles of the feet and also in the hands. (Hands and feet had always been sexually attractive to him. This is related to sexual stimulation by memories of rubbing his feet against the feet of a maid at 6 or 7 and feeling sexually stimulated when shaking hands with her.) Negro women, who previously had disgusted him, became sexually very attractive and he rubbed himself against them in crowds. He put his penis in a candlestick—an action which resembles that at 6, when he did it with another boy's penis and wanted to burn it. Together with this was a marked narcissistic development. He not only felt divine but admired his own body, put toothpaste in his hair and combed his pubic hair. In his behavior he again became mischievous, cursed easily and showed marked lack of self control. He was unable to deal with his ambivalency and ambitendency. His gestures were awkward at the height of the psychosis. As in adolescence, he again began to stare at people, trying to make them submissive, but ending up with his own submission. He showed marked passivity reactions and mystical, archaic behavior (by contortion of his own body when alone he was able to punish another student). By assuming a rigid posture (catatonic attack) he wanted to achieve perfection. His social disintegration was seen in his increasing concern about the impression he made on others and his paranoid reaction to his failure of self-assertion. (In childhood he had been in active opposition to society; in adolescence he had made a better adjustment in attitude but was less successful in making social contact.) In his day dreams he achieved social success, and he began to believe in its reality, struggling by "thinking power" with the president of the university, feeling that he would have to take over the administration.

The disorganization in thinking was marked, and was seen in the loss of ability for concrete thinking and planning, loss of discrimination and the use of vague generalities, inability to see absurdities and inability to translate from German to English (he translated word for word, while before he was able, and he has since been able, to translate German into good English with ease.) His English composition in letters suffered greatly. He frequently used slang terms and expressions of adolescence and childhood, with mistakes in grammar. His handwriting showed definite symptoms of disorganization. He was able to play on musical instruments but was unable to read music which he had learned previously. Contradictory strivings were present, without the need for an adjustment—hate toward his father and also a feeling of need for devotion; marked antagonism toward and a need to fight Gentiles, although at the same time stating that he wanted to make an adjustment to a purely Gentile group; realization of the need for discussion with the physician and yet a lack of ability and desire to do so. He frequently identified himself with others (again a feature frequently seen in adolescence), but felt also that others were able to take his personality from him. His ethical desires increased. God told him he was to lead to the path of righteousness and he felt heavily burdened.

In studying the disorganization features in this schizophrenic patient one can correlate them with previous life experiences as well as with personality features of earlier development—that is, at the time when the personality was not yet well organized (childhood and adolescence). Some of the features and problems are clearly the same as in previous

life; for instance, the sexual difficulties, the parent and emancipation problem, social leadership, behavior difficulties and philosophic implications (comparable to adolescence). Mystical experiences are also frequently noticed in adolescence, but they, as well as the more archaic experiences, are difficult to explain if one is not willing to accept the theory that reactions and conceptions of primitive people play a rôle in certain stages of our development. Thinking disorders can also occasionally be brought into close correlation with preadolescent thinking, but again this does not explain everything. Hallucinations and certain delusions of persecution would not necessarily indicate a deep-seated disorganization; they may be the outgrowth of too rigid an organization (i. e., in the paranoic patient). The cases of affective psychosis teach that either affective strain, self depreciation or the opposite, increase of belief in oneself, and the corresponding mood may facilitate and probably cause hallucinations.

It is certainly striking to notice the similarity of certain symptoms in the disorganizing schizophrenic disorder and in normal or mentally disturbed adolescence. As I have already pointed out, certain behavior disturbances are characteristic of adolescence. When one deals with an immature personality—that is, a personality which in some respects has not been organized beyond the adolescent stage—one would expect adolescent reactions also in the setting of an affective disorder. The symptoms of immaturity in such an illness are, in many respects, the same as the symptoms at the beginning of a disorganizing illness. A study of the personality will then give a lead as to whether the symptoms are due to the nonorganization of an immature make-up or to the disorganization of a fairly well organized personality. Besides the reappearance of features of adolescence and childhood, disorganization leads also to the appearance of features that are in relation to “points of fixation” in the development. This would explain certain features of the case last discussed (fetishism and the emancipation problem and anal-erotic tendencies).

A brief recapitulation of adolescent and immaturity psychoses will show their similarity to disorganization. Hypomanic states show sullen and sulky behavior, mischievousness and reaction with remorse when reprimanded, stealing of food, fear and, in addition, in the manic excitement, fantastic elaboration which is frequently presented in a playful way. The world becomes a challenge, to which the patients feel that they could respond magnificently. In their activity they show a zest for human contact and for life and aggression toward those from whom they are not emancipated. We also find social deterioration in table manners and anal-erotic manifestations.

In the depressive picture, outstanding symptoms are: sulkiness, marked sensitiveness to criticism and tactless remarks about others, a need for affection, which is not always connected with real sympathy for others, although one frequently finds also worry about the other patients. The lack of emancipation is shown by the mood description of homesickness, impulsive behavior, stubbornness, with submission to certain people, frequently childish behavior, resentfulness and revengefulness, fright felt easily, often expressed as fear of insanity, and, as an outstanding symptom, confusion, unreality and familiarity experiences. (I refer here to Kleist's cases of confusional psychosis.) Many patients feel drowsy, especially in the mornings, and express a desire to sleep the illness off, denying the need for discussion and adjustment. Sexual excitement in these cases frequently leads to misinterpretation of physical sensations in hallucinations of electricity. There are also frequently elaborate and fantastic hypochondriac concern reactions.

The easy change in mood is characteristic. One frequently notices brief hypomanic and depressive episodes, in some cases lasting only a few hours, occurring several times a day. In older people, with persistent although far less marked immaturity, this, as well as homesickness, is an outstanding symptom.

In this concept of disorganization as a basic factor of the schizophrenic illness, while regression plays an important rôle, it cannot explain all the symptoms. It is possible that what one might call regression is really of secondary importance. Owing to the disorganization of the personality, features of childhood and adolescence reappear and exert a more or less unrestricted influence. Regression appears more easily in childhood. Of many observers I shall quote only Homburger, who stated that spoiled children react to prolonged convalescence and helplessness with a relapse into the behavior of previous periods of childhood or even infancy. Faults which seemed to have been adjusted long before reappear. Especially frequent is the reappearance of bed-wetting. The frequency and easy appearance of regressive factors may therefore be explained as a part of disorganization. Narcissism, which no doubt is important, may also be only part of disorganization.

There is no proof for the conception that mystical and magic experiences and thinking are part of narcissism. There has also been too much tendency to identify these and "archaic" features with the reactions of primitive men. There are no doubt many similarities, but there is no proof that the mental development of a person is the abbreviated mental development of the human race. Genetic-dynamic investigations have yet to throw much more light on the topic. One would have to study children much more carefully to determine whether

"archaic" tendencies of childhood and adolescence influence the formation of personality. It is true that there is a lack of individualism in primitive thinking, but one finds it also in the insufficient organization of childhood. The resulting misidentification, depersonalization and identifications are therefore seen in schizophrenic, as well as in non-organization, affective psychoses. The description of Piaget in which he says that children may even believe that their thoughts can be taken away is an interesting possibility as a forerunner of passivity feelings. Schizophrenic thinking disorders are similar to the thinking of primitive people and also to that of an earlier state of development. There are not enough facts to show in what way they are related to each other. It is therefore a hasty conclusion to speak of prelogical thinking in too much of a time pattern. The vague and not sharply delimited abstractions of the schizophrenic patient appear fantastic and absurd instead of immature, because mature factors are mixed with them. A chance to study individual peculiarities of children at various stages of development might, when some schizophrenic illness later develops, lead to a better understanding of formal differences in their illnesses, e. g., motility features or disturbance of speech or thinking.

In this article I do not attempt to explain the dynamics of the schizophrenic illness, but to stress the importance of disorganizing disturbances in the personality and the fact that disorganization has to be separated from nonorganization. This differentiation naturally does not exclude the possibility of a disorganizing illness in a poorly organized personality, for instance, in psychopathic persons or in children. The diagnostic evaluation will then have to be cautious. In children it is possible only when there is a chance to follow the patient over a period of years or, if possible, to maturity.

Postpsychotic personality changes may be due to a different reorganization of the disorganized personality, but usually only features of a secondary or less important nature have been lost. Adolf Meyer spoke, therefore, of a loss of the bloom of the personality. Such a patient is not burnt out and does not become empty, but his previously hidden emptiness is now apparent. In reorganization, personality tendencies which have developed—e. g., since puberty—are still somewhere active but do not any longer occupy the dominant position which they had gradually acquired.

I do not know how to explain disorganization. It may be that constant contradictory strivings lead to a tearing apart of the insufficiently achieved organization. Some theories accept the lessening of psychic tension or the breaking of an inner tie. All this would refer to a disturbance in subject-organization, the nature and development of which have not yet been sufficiently studied. The state of disorganiza-

tion seems to be characterized by a change in the dominance of personality features and not by their anarchy. Suppressed tendencies begin to act more openly.

From the prognostic point of view one can say that nonorganization features in a pure attack (affective) psychosis will clear up with the attack. The treatment can be constructive only if one is able to organize the personality better, but this will have to be done after the psychosis has disappeared. Based on the concept of disorganization, I should hesitate to analyze too thoroughly a patient who showed definite symptoms of disorganization or who had shown them previously, and I should always be on the lookout for the reappearance of these symptoms. Otherwise one might stir up more than could be handled. If the symptoms did reappear, constructive advice and reeducation would have to be substituted for the analytic approach. A careful study of the poorly organized personality frequently causes one to moderate his expectations and prevents him from trying to attempt an impossible perfect adjustment.

#### SUMMARY

The development and degree of organization of the personality are important considerations in a genetic-dynamic approach to psychiatric problems. In the fully organized or mature person the various strivings are adjusted to one another and form part of a harmonious unit. Too loose an organization is found in the psychopathic personality; too rigid an organization leads to exaggerated features and difficulties in adjustment.

During adolescence the personality organization steadily increases; some features disappear and new features develop. Depending on the degree and stage of personality organization, one observes corresponding changes in affective psychoses. Case 1 illustrates this. The patient was studied during three manic excitements, with succeeding slight depressions at 14 and 17, and in a depression at 26.

Case 2 illustrates delayed maturing in a student, aged 19, and therefore in his depressive and hypomanic illness one finds symptoms similar to those of adolescent psychoses. During the last depression at 26 these symptoms were far less marked because of the increase in organization.

Case 3 presents the picture of a serious schizophrenic disorganization. Tendencies and features that had apparently been adjusted in this man, aged 20, reappeared and exerted a dominant influence. The disorganization of a personality can be seen not only in contradictory strivings and behavior but also in the thinking disorder, motility disturbance and mystical features. In this connection I first had to review

some of the current conceptions in schizophrenia (regression, archaic thinking).

The expressions of nonorganization in an affective psychosis are frequently mistaken for symptoms of disorganization, which they resemble. In other cases the thinking disorder and apparently incongruous features lead to the concepts of confusional and mixed manic-depressive psychoses. The understanding of nonorganization and disorganization is essential for a clear formulation of a case and influences greatly the prognosis and the therapeutic procedure.

## HEREDITY OF PATIENTS WITH PSYCHASTHENIA (JANET, RAYMOND)

### I. THE HEREDITARY FACTORS IN EIGHT HUNDRED AND NINETY CASES

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The material used for this study consists of the records of 890 patients with psychasthenia from the private practice of Dr. Hugh T. Patrick. To make clear what I mean by psychasthenia it seems advisable briefly to note the dominant symptoms. The following is a summary of those found in 50 consecutive patients. In every case organic disease was excluded.

Weakness and ready physical fatigue, 41; disturbances of sleep (the patient not falling asleep for hours, 38; early waking, 22; fitful sleep, 8; frequent sleepless nights, 5; feeling of semiconsciousness, 3; terrifying dreams, 8; excessive pre-dormal or indormescent starts, 8), 40; cardiac palpitation, 36; precordial oppression, 8; epigastric distress, 34; unpleasant sensations in the head (throbbing, fulness, tightness and pressure), often first called pain or ache, 33; periods of downheartedness, 34; frequent weeping, 29; hypersensitiveness, irritability and ready anger, 30; easy mental fatigue, 20; difficulty in "concentrating," 19; panicky spells, frequently with tremulousness, 16; full or tight feeling in the throat, 15; hypersensitiveness to noise, 15; occasional death wishes, 14; feeling of impending syncope, 14; anorexia, 13; asthenopia, 2; sensitiveness to poor ventilation, 8; occasional numb feeling in extremities, 5; feeling of inspiration "not going deep enough," 4; giddiness, 3; flushing of the face, 3; tingling, 3; tremor of hands, 3; attacks of sweating, 3; simple regurgitation, 2; diminished sex desire, 2; premature ejaculation, 2; twitchings, 2.

Thirty-one patients had definite phobias, frequently not spontaneously avowed, sometimes scarcely known to the patient himself. Obviously, many of the aforementioned symptoms were the result of fear. The patient complained of the symptom; the fear had to be brought to light. Of the 31 patients, 23 feared mental disorder and 21 physical disease, mostly cardiac or cerebral. Twenty-eight had some form of agoraphobia and 27 fear of impending death or collapse. Other fears were: of choking, 4; of injuring self or others, or of sharp instruments, 6; of death in sleep, 1; in every instance a logical origin of the phobia was found.

Forty-six of the patients had passed through a period of mental (emotional) stress shortly before the onset of the principal symptoms.

The disorder outlined obviously has gone under different labels at different times and in different hands; probably most frequently under

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that of neurasthenia,<sup>1</sup> a diagnosis now infrequently made. Hypochondria, anxiety neurosis, imperative ideas, even occasionally hysteria, are terms applied to these psychoneuroses. Probably "maladjustment" covers many of them. Although keenly aware that psychasthenia<sup>2</sup> is an unsatisfactory diagnosis in many instances, I believe that it is the best designation for these disorders, and consequently it is adopted in this article.

Practically all writers on psychasthenia<sup>3</sup> agree that heredity plays an important rôle in its etiology, but few precise studies of this factor have been made. Apparently writers have based their opinion on the observation of relatively few cases or on the statements of others. I have been able to find but scant and conflicting statistical data on this subject.

In 1872, Gull and Ainstie<sup>4</sup> stated that in the antecedents of these patients, in an immense number of the cases if not in all, psychoses occurred. Beard<sup>5</sup> wrote that this disorder is hereditary, and Levillain,<sup>6</sup> that heredity predisposes one to it. Blocq<sup>7</sup> stated that in its serious forms it is most often of hereditary origin, but that there are certain cases that develop in a soil intact from all nervous taint. Gowers<sup>8</sup> said that the predisposition often lies in individual temperament, which may be the result of neurotic inheritance, and that the most severe forms occur in persons whose family presents a tendency to mental diseases. Von Hösslin<sup>9</sup> found evidences of neuropathic heredity in 286 of 828

1. For a discussion of the present status of the term neurasthenia, see Bassoe, P.: *The Origin, Rise and Decline of the Neurasthenia Concept*, Wisconsin M. J. **27**:11 (Jan.) 1928. Bassoe is of the opinion that the term neurasthenia has been so abused that it ought to be dropped from medical nomenclature. With this view, the present writer is in accord.

2. Janet, P.: *Les obsessions et la psychasthénie*, Paris, Félix Alcan, 1903. Janet, P., and Raymond, F.: *Les obsessions et la psychasthénie*, Paris, Félix Alcan, 1903.

3. In the references to the literature subsequently given in this paper, not so much attention was paid to the label as to the symptoms which the various writers described. In all cases, regardless of what name the writer used, the symptoms were similar to those considered here as constituting psychasthenia.

4. Gull, W. W., and Ainstie, F. E.: Hypochondriasis, in Reynold, J. R.: *System of Medicine*, Philadelphia, J. B. Lippincott Company, 1872, vol. 2.

5. Beard, G. M.: *A Practical Treatise on Nervous Exhaustion*, New York, William Wood and Company, 1880.

6. Levillain, F.: *La neurasthénie*, Paris, A. Maloine, 1891.

7. Blocq, Paul: *Neurasthenia*, *Brain* **14**:306, 1891.

8. Gowers, W. R.: *A Manual of Diseases of the Nervous System*, London, J. & A. Churchill, 1893, vol. 2.

9. von Hösslin, R.: *Handbuch der Neurasthenie*, Leipzig, F. C. W. Vogel, 1893.

cases, or 34.5 per cent. Magnan and Legrain<sup>10</sup> stated that this syndrome is inherited in the great majority of cases. Of 250 men and 250 women with this disorder, Krafft-Ebing<sup>11</sup> found evidences of a neuropathic taint in 151 men and 167 women (63.6 per cent). Freud<sup>12</sup> wrote that in this neurosis heredity is potent in all cases, and plays the star rôle in the majority. Legrand du Saulle<sup>13</sup> placed heredity first among the predisposing causes, and Saury<sup>14</sup> asserted, "He who speaks of psychasthenia speaks of heredity." Pitres and Régis<sup>15</sup> found some evidence of a familial neuropathy in 80 per cent of their cases, and Janet in 117 of 170 cases studied (68.8 per cent). Binswanger and Siemerling<sup>16</sup> thought that the most important prerequisite was a neuropathic tendency. Dubois<sup>17</sup> said, "Psychasthenia is always congenital by virtue of that heredity which outlines the characteristics of our brain." Loewenfeld<sup>18</sup> said that this disorder was based on hereditary predisposition, which serves to accentuate the influence of exciting agencies. Raymond<sup>19</sup> believed the most important cause to be heredity, similar or dissimilar, and with this Strümpell<sup>20</sup> agreed. Cramer<sup>21</sup> believed the antecedents nearly always to be psychopathic persons, and Dercum<sup>22</sup> emphasized the frequency of minor and (or) major nervous diseases in the family. Oppenheim<sup>23</sup> stated that the graver forms of this disorder always spring from neuropathic heredity,

10. Magnan and Legrain: *Les dégénérés (état mental et syndromes épileptiques)*, Paris, Rueff & Cie, 1895.

11. Krafft-Ebing, R.: *Nervosität und neurasthenische Zustände*, in *Nothnagel, C. W. H.: Spezielle Pathologie und Therapie*, Vienna, Alfred Hölder, 1895.

12. Freud, S.: *L'hérédité des neuroses*, in *Sammlung kleiner Schriften zur Neurosenlehre*, Vienna, Franz Deuticke, 1906.

13. Legrand du Saulle, quoted by Janet.<sup>1</sup>

14. Saury, M., quoted by Janet.<sup>1</sup>

15. Pitres and Régis, quoted by Janet.<sup>1</sup>

16. Binswanger, O., and Siemerling, E.: *Lehrbuch der Psychiatrie*, Jena, Gustav Fischer, 1904.

17. Dubois, P.: *The Psychic Treatment of Nervous Disorders*, translated and edited by Smith Ely Jelliffe and W. A. White, New York, Funk & Wagnalls Company, 1905.

18. Loewenfeld, L.: *Die moderne Behandlung der Nervenschwäche (Neurasthenie)*, der Hysterie und verwandter Leiden, Wiesbaden, J. F. Bergmann, 1904.

19. Raymond, F.: *Neuroses et psychoneuroses*, Paris, Delarue, 1907.

20. Strümpell, A.: *A Text Book of Medicine*, translated by H. F. Vickery and C. P. Knapp, New York, D. Appleton and Company, 1911.

21. Cramer, A.: *Die Neurasthenie*, in *Lewandowsky: Handbuch der Neurologie*, Berlin, Julius Springer, 1914, vol. 5.

22. Dercum, F. X.: *A Clinical Manual of Mental Diseases*, Philadelphia, W. B. Saunders Company, 1917.

23. Oppenheim, H.: *Lehrbuch der Nervenkrankheiten*, ed. 7, Berlin, S. Karger, 1923.

and Bleuler,<sup>24</sup> that the first cause is hereditary neurotic predisposition. Craig and Beaton<sup>25</sup> practically agreed. Alfred Adler<sup>26</sup> dissented from the views of practically all other writers, believing that the malevolence of heredity has been greatly exaggerated. Neustadter<sup>27</sup> said that heredity is the most important cause of psychasthenia, and Wechsler,<sup>28</sup> that all theories, including psychoanalysis, assume some sort of constitutional predisposition, some hereditary factors, as the fertile soil in which neuroses take root.

Of the aforementioned writers, only von Hösslin, Krafft-Ebing, Pitres and Régis, and Janet have given statistical data in support of their views.

In my series of 890 cases there was a definite history of a familial neuropathic tendency<sup>29</sup> in 676 cases, or 76 per cent. In the remaining 214 cases, the family history was entirely negative in this respect. This value varies considerably from those previously mentioned.

In my series a neuropathic factor was found in the direct line (parents) in 70.9 per cent of the cases; in the indirect line alone (grandparents, uncles, aunts and cousins) in 1.6 per cent, and in siblings alone in 3.5 per cent.

Table 1 shows the neuropathic features found in the direct line (parents), the method of compilation advocated by Koller<sup>30</sup> and Diem<sup>31</sup> being used. A study of this table shows that the most frequent neuropathic manifestation in the parents was a nervous disorder; this was found in 51.1 per cent of the cases. Of these nervous disorders, "nervousness" was the most frequent, 24.6 per cent; migraine came next, 21.6 per cent. Similar heredity, i. e., psychasthenia in a parent, was relatively rare, 3.6 per cent. Still rarer were hysteria, 0.5 per cent, and epilepsy, 0.5 per cent. A functional psychosis was found in

24. Bleuler, E.: *Text Book of Psychiatry*, translated by A. A. Brill, New York, The Macmillan Company, 1924.

25. Craig, M., and Beaton, T.: *Psychological Medicine*, London, J. & A. Churchill, 1926.

26. Adler, A.: *Problems of Neuroses*, London, Kegan, Paul, Trench, Trubner and Co., 1929.

27. Neustadter, M.: *Text Book of Clinical Neurology*, Philadelphia, F. A. Davis Company, 1929.

28. Wechsler, I.: *The Neuroses*, Philadelphia, W. B. Saunders Company, 1929.

29. The neuropathic features found in my series were nervousness, migraine, psychasthenia, hysteria, functional psychosis, epilepsy, senile psychosis, suicide, alcoholism, fainting spells, apoplexy, writer's cramp, defective mental development, psychopathic personality.

30. Koller, J.: *Beitrag zur Erblichkeits-Statistik der Geisteskranken in Canton Zurich: Vergleichung derselben mit der erblichen Belastung gesunder Menschen durch Geistestörungen*, *Arch. f. Psychiat.* **27**:268, 1895.

31. Diem, O.: *Die psychoneurotische erbliche Belastung der Geistesgesunden und der Geisteskranken*, *Arch. f. Rassen- u. Gesellsch. Biol.* **2**:215, 1905.

the parents in 5.6 per cent of the cases; apoplexy (strictly speaking, not a nervous or mental disease) in 9.9 per cent; senile psychosis, psychopathic personality and suicide were relatively rare in the parents, being 0.2, 0.9 and 0.3 per cent, respectively.

#### NATURE AND DISTRIBUTION OF NEUROPATHIC TRAITS IN RELATIVES OF PATIENTS WITH PSYCHASTHENIA

In my series, the 890 patients had 1,648 relatives in whom a neuropathic taint was found. These traits had the following distribution:

Nervousness was found in 872 relatives; psychasthenia in 67, psychosis in 128, senile psychosis in 4, alcoholism in 33, apoplexy (not strictly a nervous or mental

TABLE 1.—*Percentage of Patients with Psychasthenia in Which the Various Neuropathic Factors Occurred in the Direct Line (Parents)*

Psychosis	Nervous Disorders	Alcoholism	Apoplexy	Senile Psychosis	Psychopathic Personality	Suicide
5.6	51.1*	2.9	9.9	0.2	0.9	0.3

\* Of these 24.6 were cases of nervousness; 21.6, of migraine; 3.6, of psychasthenia; 0.3, of fainting spells; 0.5, of hysteria, and 0.5, of epilepsy.

TABLE 2.—*Percentage Distribution of Neuropathy Among 1,648 Tainted Relatives of 890 Patients with Psychasthenia*

Psychosis, per Cent	Nervous Disorders, per Cent	Alcoholism, per Cent	Apoplexy, per Cent	Senile Psychosis, per Cent	Psychopathic Personality, per Cent	Suicide, per Cent
7.8	82.5*	2.0	5.6	0.2	1.3	0.6

\* Of these 52.9 per cent were cases of nervousness; 22.7 per cent, of migraine; 4.1 per cent, of psychasthenia; 0.4 per cent, of hysteria; 1.2 per cent, of epilepsy; 0.2 per cent, of fainting spells; 0.1 per cent, of writer's cramp; 0.8 per cent, of feeble-mindedness, and 0.1 per cent, of tic.

disorder, but included here in order to conform with the method of Diem and Koller) in 93, feeble-mindedness (strictly speaking, neither a psychosis nor a nervous disorder, but included here for the sake of convenience) in 14, migraine in 374, hysteria in 6, epilepsy in 19, suicide in 10, fainting spells in 3, writer's cramp in 2, psychopathic personality in 21 and tic in 2.

In table 2 these figures are expressed in terms of percentages. A study of the table shows that in the neuropathically tainted relatives of patients with psychasthenia, nervous disorders show an overwhelming majority (82.5 per cent). Psychosis is the next most frequent (7.8 per cent). Alcoholism, apoplexy, senile psychosis, psychopathic personality and suicide are relatively uncommon (2 per cent, 5.6 per cent, 0.2 per cent, 1.3 per cent and 0.6 per cent, respectively).

## SUMMARY

Although nearly all writers on psychasthenia state that heredity plays an important rôle in the etiology of this disorder, the statements generally remain unsupported by definite studies of a large number of cases.

The hereditary factors found in 890 cases of psychasthenia are presented. Six hundred and seventy-six patients (76 per cent) had a history of a more or less familial neuropathic tendency. In 70.9 per cent this tendency was found in the parents. The most frequent neuropathic element in the parents was a nervous disorder (51.1 per cent). Functional psychosis in the parents was much less frequent (5.6 per cent). Parental suicide, senile psychosis and suicide were relatively infrequent. Apoplexy was found in the parents not infrequently (9.9 per cent). The 890 patients with psychasthenia had 1,648 relatives exhibiting a neuropathy. In these, nervous disorders were by far the most common (82.5 per cent); psychosis was second in frequency (7.8 per cent). In the relatives with a neuropathic taint, alcoholism, senile psychosis, psychopathic personality and suicide were relatively uncommon (2.0 per cent, 0.2 per cent, 1.3 per cent and 0.6 per cent, respectively). Apoplexy in these relatives was not infrequent (5.6 per cent).

## HEREDITY OF PATIENTS WITH PSYCHASTHENIA (JANET, RAYMOND)

### II. COMPARISON WITH HEREDITY OF PERSONS IN GOOD MENTAL HEALTH

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In a previous communication<sup>1</sup> I pointed out that although practically all writers agree that heredity plays an important rôle in the etiology of psychasthenia, few, if any, precise studies have been made to substantiate this view. I then presented a statistical formulation of the hereditary neuropathic elements in 890 patients with psychasthenia from the private practice of Dr. Hugh T. Patrick. It must be remembered that the presence of neuropathy in the relatives of patients with psychasthenia is not by itself evidence that neuropathic heredity is of etiologic significance, a view which all writers appear to accept. Persons in good mental health come from stock that has its burden of neuropathy; so before hereditary factors can be considered significant in the etiology of psychasthenia, it must be demonstrated that such patients come of a stock tainted more heavily than or differently from that of persons in good mental health. The present study has for its object the determination of differences or similarities between the heredity of patients with psychasthenia and that of persons in good mental health.

Data regarding the hereditary neuropathic elements in persons in good mental health have been published by Diem,<sup>2</sup> who studied these factors in 1,193 persons. As far as I have been able to determine, his are the only data available on this point. To determine differences between the hereditary factors in patients with psychasthenia and persons in good mental health, I shall compare my findings in psychasthenic persons with those of Diem<sup>3</sup> in normal persons.

From the Department of Nervous and Mental Diseases, Northwestern University Medical School. The material used for this study consists of 890 cases of psychasthenia from the private practice of Dr. Hugh T. Patrick.

1. Paskind, Harry A.: Heredity of Patients with Psychasthenia (Janet, Raymond): I. The Hereditary Factors in Eight Hundred and Ninety Cases, this issue, page 1305.

2. Diem, O.: Die psycho-neurotische-erbliche Belastung der Geistesgesunden und der Geisteskranken, Arch. f. Rassen-u. Gesellsch.-Biol. **2**:215, 1905.

3. Diem considered functional psychosis, neurasthenia, nervousness, hysteria, epilepsy, traumatic neurosis, fear neurosis, migraine, chorea, enuresis, paralysis agitans, alcoholism, apoplexy, senile psychosis and suicide as evidences of a neuropathic tendency.

Table 1 shows the percentage of cases in which a familial neuropathic factor was detected in psychasthenic patients as compared with similar data in Diem's normal persons. A familial neuropathic trend was found in 76 per cent of patients with psychasthenia; in Diem's normal persons this trend was found in 67 per cent. In patients with psychasthenia, parental neuropathy was found in 70.9 per cent; in Diem's series, in only 33 per cent. In the indirect line (grandparents, uncles, aunts and cousins), persons in good mental health showed a greater

TABLE 1.—Percentage of Incidence of a Neuropathic Taint in Patients with Psychasthenia, Compared with That of Persons in Good Mental Health, Showing the Proportion Tainted Through the Direct Line (Parents), Indirect Line (Grandparents, Uncles, Aunts and Cousins) and Siblings

Incidence of Neuropathic Taint	Patients with Psychasthenia (Present Series, 890 Cases), per Cent	Persons in Good Mental Health (Diem, 1,193 Cases), per Cent
In the family.....	76	67
In the direct line.....	70.9	33
In the indirect line.....	1.6	29
In siblings only.....	3.5	5

TABLE 2.—Percentage of Patients with Psychasthenia in Which the Various Neuropathic Factors Occurred in the Direct Line (Parents), Compared with Similar Data for Persons in Good Mental Health

	Psy- chosis	Nervous Disorders	Alco- holism	Apo- plexy	Senile Psy- chosis	Psycho- pathic Person- ality	Suicide
Patients with psychasthenia (present series, 890 cases).....	5.6	51.1*	2.9	9.9	0.2	0.9	0.3
Persons in good mental health (Diem, 1,193 cases).....	2.2	5.7	11.2	5.9	1.4	5.9	0.4

\* Of these, 24.6 were cases of nervousness; 3.6, of psychasthenia; 0.5, of hysteria; 21.6, of migraine; 0.3, of fainting spells, and 0.5, of epilepsy.

tainting than did patients with psychasthenia, 29 per cent and 1.6 per cent, respectively. In the two groups no significant differences were found in neuropathy occurring in siblings alone; 3.5 per cent of cases occurred in patients with psychasthenia, and 5 per cent in Diem's series.

In table 2 is shown the percentage of psychasthenic patients in which the various neuropathic features occurred in the parents, as compared with similar data in Diem's mentally normal persons. It shows some interesting differences. In patients with psychasthenia a psychosis was found in a parent in 5.6 per cent; in persons in good mental health, in 2.2 per cent. Nervous disorders were almost ten times as frequent

in the parents of my patients as they were in those of Diem's normal persons, 51.1 per cent in the former and 5.7 per cent in the latter. In Diem's series, parental alcoholism, senile psychosis and psychopathic personality were more frequent than in mine; parental suicide shows no striking difference. Apoplexy was found much more frequently in the parents of patients with psychasthenia than in Diem's series, 9.9 per cent as compared with 5.9 per cent.

In table 3 is shown the percentage distribution of neuropathy in the relatives of patients with psychasthenia as compared with Diem's material. The most striking difference here is in the frequency of

TABLE 3.—*Percentage Distribution of the Various Neuropathies Among the Neuropathically Tainted Relatives of Patients with Psychasthenia Compared with That of Persons in Good Mental Health*

	Psy- chosis, per Cent	Nervous Disorders, per Cent	Alco- holism, per Cent	Apo- plexy, per Cent	Senile Psy- chosis, per Cent	Psycho- pathic Person- ality, per Cent	Suicide, per Cent
Patients with psychasthenia (present series, 1,648 neuropathic factors in 896 cases).....	7.8	82.5*	2.0	5.6	0.2	1.3	0.6
Persons in good health (Diem, 1,945 neuropathic factors in 1,193 cases).....	15.1	14.9	21.3	18.4	7.4	21.3	1.6

\* Of these, 52.9 per cent were cases of nervousness; 22.7 per cent, of migraine; 4.1 per cent, of psychasthenia; 0.4 per cent, of hysteria; 1.2 per cent, of epilepsy; 0.2 per cent, of fainting spells; 0.1 per cent, of writer's cramp; 0.8 per cent, of feeble-mindedness, and 0.1 per cent, of tic.

nervous disorders: 82.5 per cent in my series and 14.9 per cent in Diem's. The tainted relatives of Diem's subjects showed more psychosis than did those of the psychasthenic patients, 15.1 per cent and 7.8 per cent, respectively. In Diem's series alcoholism, apoplexy, senile psychosis, psychopathic personality and suicide were more common than in mine. This table shows, however, that, as compared with the relatives of mentally well people, the relatives of patients with psychasthenia are overwhelmingly tainted with nervous disorders.

#### SUMMARY

The hereditary neuropathic factors in psychasthenic patients are compared with the same factors in persons of good mental health. The comparison reveals significant differences. Because of these differences it may be postulated with certainty that hereditary factors play a rôle in the etiology of psychasthenia.

## HEREDITY OF PATIENTS WITH PSYCHASTHENIA (JANET, RAYMOND)

### III. COMPARISON OF THE HEREDITY OF PSYCHASTHENIC PATIENTS WITH THAT OF SCHIZOPHRENIC PATIENTS AND PERSONS WITH MANIC-DEPRESSIVE PSYCHOSIS

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In a previous communication,<sup>1</sup> based on a study of 890 patients with psychasthenia in the private practice of Dr. Hugh T. Patrick, I presented a statistical formulation of the hereditary factors in this disorder. In a second communication<sup>2</sup> I presented data showing that patients with psychasthenia have a hereditary endowment different from that of persons in good mental health. The question naturally follows: Do patients with schizophrenia and with manic-depressive psychosis present differences in heredity from that of patients with psychasthenia? Does the more benign psychasthenia arise from the same or from a different hereditary subsoil than do manic-depressive psychosis and schizophrenia? The present study is concerned with this question.

Data regarding the hereditary factors in manic-depressive psychosis have been made available by Sünner,<sup>3</sup> for the more malignant institutional type, and by myself,<sup>4</sup> for the more benign extramural type seen in private practice. Data regarding hereditary relations in schizophrenia have been published by Barrett.<sup>5</sup> In this study the hereditary factors in patients with psychasthenia will be compared with the data given by these writers.

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From the Department of Nervous and Mental Diseases, Northwestern University Medical School.

1. Paskind, Harry A.: Heredity of Patients with Psychasthenia (Janet, Raymond): I. The Hereditary Factor in Eight Hundred and Ninety Cases, this issue, p. 1305.

2. Paskind, Harry A.: Heredity of Patients with Psychasthenia (Janet, Raymond): II. Comparison with the Heredity of Persons in Good Mental Health, this issue, page 1311.

3. Sünner, Paul: Die psychoneurotische erbliche Belastung bei dem manisch-depressiven Irresein, auf Grund der Diem Kollerschen Belastungsberechnung, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **77**:453, 1922.

4. Paskind, Harry A.: Hereditary Factors in Manic-Depressive Psychosis, *Arch. Neurol. & Psychiat.* **24**:747 (Oct.) 1930.

5. Barrett, A. M.: "Heredity Relations in Schizophrenia," in Dana, C. L., and others: *Schizophrenia*, Association for Research in Nervous and Mental Disease, New York, Paul B. Hoeber, 1928, vol. 5.

A familial neuropathic taint was found in 76 per cent of patients with psychasthenia. How this compares with similar data in manic-depressive psychosis and in schizophrenia is shown in table 1. Of patients with institutional manic-depressive psychosis, a neuropathic tendency was found in 84.13 per cent; of patients with extramural manic-depressive psychosis, in 83.2 per cent, and of schizophrenic patients, in 78.01 per cent. It appears, then, that a neuropathic tendency is slightly less frequent in psychasthenia than in the psychoses mentioned. In psychasthenia neuropathy was found in the direct line of the patients (parents) in 70.9 per cent of the cases (table 1). In this regard psychasthenic patients differ from schizophrenic patients and from those with manic-depressive psychosis. In schizophrenic patients a parental neuropathy was found in 34.66 per cent; in patients

TABLE 1.—Percentage Incidence of a Neuropathic Taint in Patients with Psychasthenia as Compared with That of Patients with Manic-Depressive Psychosis and with Schizophrenia, Showing the Proportion Tainted Through the Direct Line (Parents), Indirect Line (Grandparents, Uncles, Aunts and Cousins) and Through Siblings

History of Neuropathy	Patients with Psychasthenia; (This Series, 890 Cases) per Cent	Patients with Institutional Manic-Depressive Psychosis (Sünnér, 650 Cases) per Cent	Patients with Extramural Manic-Depressive Psychosis (Paskind, 485 Cases) per Cent	Schizophrenia (Barrett, 150 Cases) per Cent
In family.....	76.00	84.13	83.20	78.01
In the direct line.....	70.90	65.53	67.90	34.66
In the indirect line.....	1.60	14.76	6.20	38.68
In siblings only.....	3.50	4.76	9.10	4.67

with institutional manic-depressive psychosis, in 65.53 per cent, and in extramural patients with manic-depressive psychosis, in 67.9 per cent. A neuropathy in the indirect line (grandparents, uncles, aunts and cousins) was found in 1.6 per cent of psychasthenic patients (table 1). They differ in this respect from manic-depressive and from schizophrenic patients. This type of tainting was found in 14.76 per cent of institutional patients with manic-depressive psychosis, in 6.2 per cent of extramural patients with manic-depressive psychosis and in 38.68 per cent of schizophrenic patients. Neuropathy in siblings only is lowest in psychasthenia (table 1). It appears, then, that in psychasthenia a smaller percentage of patients show a neuropathic heredity, and in addition there is a marked difference in the position of that heredity. In psychasthenia the neuropathic taint is dominant in the direct line, and less evident in the indirect line and in siblings.

Table 2 shows the percentage of psychasthenic patients whose various neuropathic features occurred in the parents, as compared with similar data for patients with manic-depressive psychosis and with

schizophrenia. This table shows some interesting differences in heredity between psychasthenia and the other disorders. In psychasthenia, a psychosis was found in a parent in 5.6 per cent of cases. In institutional patients with manic-depressive psychosis, this ratio is 18.92 per cent and in extramural patients 23.3 per cent and in schizophrenia, 14.66 per cent. On the other hand, parental nervous disorder is much more

TABLE 2.—Percentage of Patients with Psychasthenia in Whom the Various Neuropathic Features Occurred in the Direct Line (Parents) as Compared with Similar Data for Patients with Manic-Depressive Psychosis and Schizophrenia

	Psy- chosis	Nervous Disorders	Alco- holism	Apo- plexy	Senile Psy- chosis	Psycho- pathic Person- ality	Suicide
Patients with psychasthenia (present series, 890 cases).....	5.60	51.10	2.90	9.90	0.20	0.90	0.30
Institutional patients with manic-depressive psychosis (Sünder, 650 cases).....	18.92	14.00	11.38	8.15	2.15	9.38	1.53
Extramural patients with manic-depressive psychosis (Paskind, 485 cases).....	23.30	40.70	2.80	....	....	0.70	1.20
Schizophrenia (Barrett, 150 cases) .....	14.66	1.33	9.33	0.67	....	8.67	....

TABLE 3.—Percentage Distribution of the Various Neuropathies Among the Neuropathically Tainted Relatives of Patients with Psychasthenia Compared with That of the Relatives of Patients with Manic-Depressive Psychosis and Schizophrenia

	Psy- chosis, per Cent	Nervous Disorders, per Cent	Alco- holism, per Cent	Apo- plexy, per Cent	Senile Psy- chosis, per Cent	Psycho- pathic Person- ality, per Cent	Suicide, per Cent
Patients with psychasthenia (present series, 1,648 factors in 890 cases).....	7.80	82.70	2.00	5.60	0.20	1.30	0.60
Institutional patients with manic-depressive psychosis (Sünder, 1,199 factors in 650 cases) .....	43.86	15.10	9.80	11.80	3.00	11.50	4.80
Extramural patients with manic-depressive psychosis (Paskind, 877 factors in 485 cases) .....	35.00	59.50	2.90	.....	.....	0.30	2.10
Schizophrenia (Barrett, 273 factors in 150 cases).....	43.22	4.76	11.36	14.65	1.83	21.24	2.93

frequent in psychasthenia (51.1 per cent) than it is in manic-depressive psychosis (14 per cent in institutional patients and 40.7 per cent in noninstitutional patients) and in schizophrenia (1.33 per cent). That is, in psychasthenia the predominating parental neuropathy is nervous disorder; in manic-depressive psychosis and in schizophrenia, it is psychosis.

In table 3 is shown the percentage distribution of the various neuropathies among the tainted relatives of patients with psychasthenia as compared with that among the relatives of patients with manic-depressive psychosis and with schizophrenia. A psychosis was found in only 7.8 per cent of the tainted relatives of psychasthenic patients, in 43.8 per cent of those of institutional patients with manic-depressive psychosis, in 35 per cent of those of extramural patients with manic-depressive psychosis and in 43.22 per cent of those of schizophrenic patients. In contrast, a nervous disorder was found in 82.5 per cent of the tainted relatives of psychasthenic patients, while in those of institutional patients with manic-depressive psychosis it was 15.1 per cent; in those of extramural patients with manic-depressive psychosis, 59.5 per cent, and in those of schizophrenic patients, 4.76 per cent. Tainted relatives of patients with psychasthenia showed less alcoholism, less apoplexy, less senile psychosis and less suicide than did those of patients with manic-depressive psychosis and schizophrenia. Psychopathic personality was less frequent in the relatives of psychasthenic patients than in those of institutional patients with manic-depressive psychosis and in those of schizophrenic patients.

#### SUMMARY

The hereditary factors in psychasthenia are compared with those found in manic-depressive psychosis and in schizophrenia; marked differences are found. In psychasthenia fewer cases show a hereditary neuropathic taint, and the taint is more frequent in the direct line and less frequent in the indirect line and siblings than in the other two conditions. In psychasthenia parental nervous disorder is the predominating neuropathy; in the psychoses mentioned parental psychosis is the predominating neuropathy. In the tainted relatives of patients with psychasthenia, nervous disorder predominates, in those of patients with the psychoses mentioned, psychosis is the predominating neuropathy. These differences lend support to a view that psychasthenia is fundamentally (nosologically) different from manic-depressive psychosis and schizophrenia.

## CEREBRAL ANGIOGRAPHY WITH THOROTRAST

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The procedure of arterial encephalography has encountered certain difficulties in its general adoption. Operators have feared to puncture the carotid and above all to inject sodium iodide to obtain opacity of the arteries. In my book I<sup>1</sup> record the studies carried out in connection with arterial encephalography, and I analyze the accidents attendant on the procedure. To quote from this publication:

From our first cerebral arteriography by the injection of 25 per cent sodium iodide into the internal carotid (June, 1927) to the present time, we have had a few complications. In short, we have observed, following the intracarotid injection, occasional hemiplegia, which has disappeared three or four days later. More frequently, we have seen short epileptic seizures which have become more rare and, above all, less forceful since the adoption of the administration of phenobarbital.

But this aspect of the problem raises doubt and prejudice in the minds of neurologists.

I have also expressed the opinion that the test is dangerous in cases of arteriosclerosis, among which there have been two deaths, and although my statistics of three hundred and fifty cases show a total mortality of less than 1.5 per cent, the distrust persists. It is because of this fact that I was induced to try another substance which, although quite as opaque to the x-rays as 25 per cent sodium iodide, does not produce the least reaction in the patient. Abrodil, because of its composition, had the same disadvantages as sodium iodide, as I have verified in a series of cases. I have, therefore, studied thorotrast, which had previously been employed at Lisbon with success in arteriography of the extremities.

The problem of cerebral arteriography was, however, quite different. One had to find a substance that would produce in the vessels of the brain an opacity greater than that of the bones of the cranium and thus make the circulation visible. I began by making hypodermic injections of thorotrast, 25 per cent. They were not at all painful, and to the x-rays the opaque spot was, in general, more opaque than the bones

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Translated from the French by Lyle Gage, Montreal, Canada. A summary of a previous contribution to the same subject appears under Abstracts from Current Literature in this issue, page 1346.

1. Egas, Moniz: *Diagnostic des tumeurs cérébrales et épreuve de l'encéphalographie artérielle*, Paris, Masson & Cie, 1931.

of the extremities. On continuing the study, I injected small doses of the same substance into the common carotid without the least reaction. I have increased the doses successively and have proved that from 8 to 10 cc. of thorotrast do not cause the least disturbance. After the procedure the patients are able to get up and walk without any inconvenience.

The cerebral arteriograms obtained with thorotrast are just as definite as those obtained with sodium iodide (fig. 1). Figures 2 and 3 show arteriographic pictures of a woman with a median tumor of the

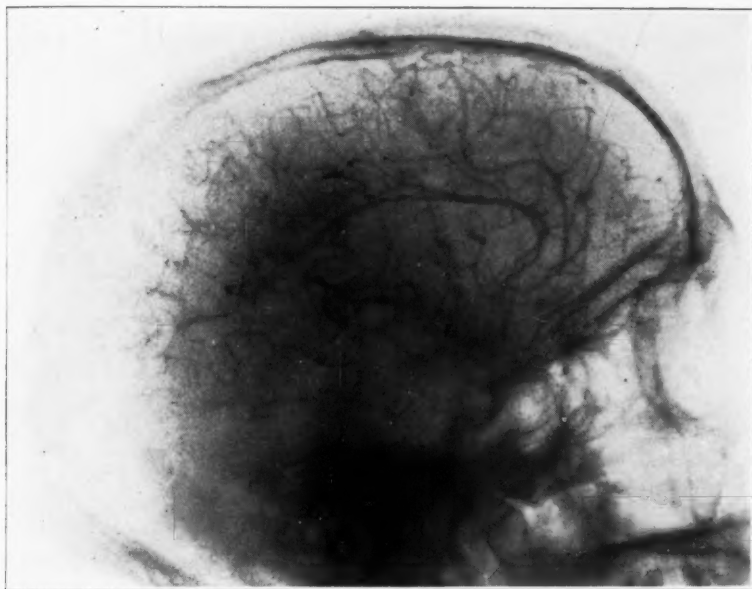


Fig. 1.—Normal arteriogram produced with the injection of thorotrast into the internal carotid.

base of the left frontal lobe. The neurologic diagnosis was that of a tumor in the chiasmatic region (destruction of the sella turcica, exophthalmos and lateral reduction of one of the visual fields).

In this case I made a second injection at the same sitting in order to obtain a picture in the occipitofrontal position, and had perfect radiographic success.

I do not believe that the test should be carried out with the unexposed carotid, even with an inoffensive substance like thorotrast, because of the dangers of extravasation. In the majority of cases it is necessary to expose the common carotid in order to inject the substance into it more accurately. The introduction of the needle is not always

easy, in spite of the size of the common carotid, and one must not make an injection without being sure that the needle has entered well into the lumen of the artery. This is the indispensable condition for obtaining cerebral arteriograms.

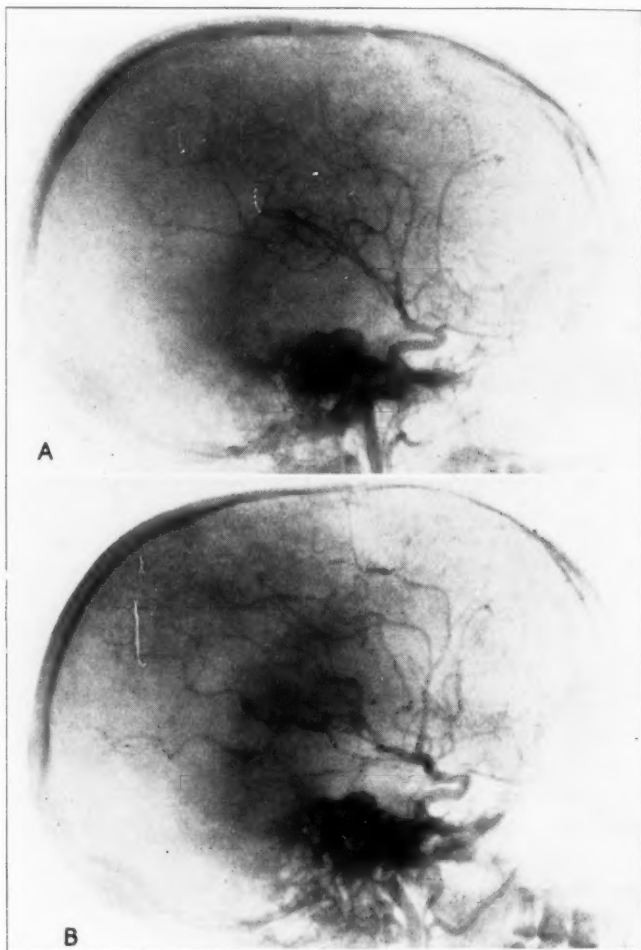


Fig. 2.—*A*, arteriography on the left side obtained with thorotrast. A tumor of the frontal region is displacing the carotid trunk and the cerebral artery backward. *B*, arteriography on the right side. Displacement similar to that in *A* is shown. It was concluded that the patient had a tumor in the median position, involving both frontal lobes.

The injection should be made with the greatest speed. For this purpose I prefer a syringe of the record type with wings that fit the

hand well. The force necessary for the injection of thorotrast, a somewhat viscid liquid, is greater than that used with the iodide solution.

I always make the injection into the right carotid if the substance is to be injected on only one side, but usually the injection into the carotid and the angiography are carried out on both sides.

Thorotrast is not soluble in the blood and can be seen in the entire cerebral circulation—in the arteries, capillaries and veins. In its passage through the capillaries the blood-thorotrast mixture produces a shadow which precedes the appearance of opacity in the venous circula-

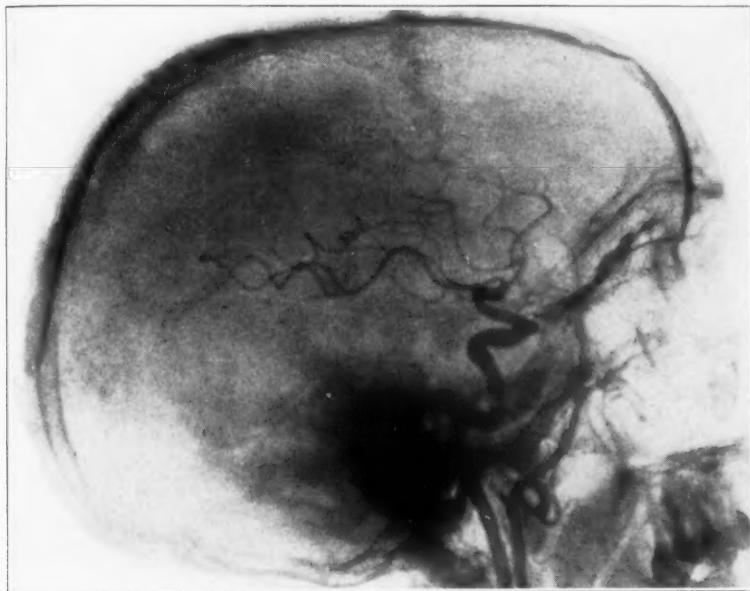


Fig. 3.—Arterial encephalography in a case of cerebral arteriosclerosis, showing the typical appearance of carotid branching.

tion. This shadow, a characteristic network, appears in the first phase, which is fleeting.

The second phase follows immediately on the first and in it is seen the shadow of the thorotrast in the veins, the blood-thorotrast mixture not having reached the internal jugular.

The phlebogram presented in figure 4, taken four seconds after an injection of 15 cc. of thorotrast into the common carotid, shows the superficial veins, the ascending veins, the vein of Trolard, the vein of Labbé, the deep veins, the trunk of Galen, the vein of Galen and the basic vein, as well as the straight, the lateral, the superior longitudinal and the inferior longitudinal sinuses and the torcula Herophili.

As the different phases of the circulation have been seen by means of the shadow of the passing thorotrast, I have succeeded in recording the speed of the circulation in the brain, the meninges and the rest of the head and face. By this arteriophlebographic method I have found that the speed of circulation is much greater in the brain than in other parts of the head, although these regions are at similar distances from the heart. I have recently been able to confirm these facts by obtaining photographs of the circulation in the head. Six angiograms have been made in from six to seven seconds with the aid of "radio-carrousel," just invented by my colleague, Dr. Pereira Caldas, a radiologist.



Fig. 4.—Phlebogram, showing the superficial and deep veins. It was taken four seconds after the injection of 15 cc. of thorotrast into the common carotid.

I have been able to show not only the differences in the speed of the circulation at various points, but also the manner in which the thorotrast behaves. In the capillaries of the brain it disappears immediately and leaves no trace, but in the capillaries elsewhere in the head it is temporarily delayed for from one to two hours.

In conclusion, the operation of injection into the carotid and angiography is carried out on both sides, that is, injection into the two common carotids in one session. The procedure is harmless, involves no inconvenience for the patient and hastens the localizing diagnosis of tumors of the brain.

Patients with arteriosclerosis stand the test of cerebral angiography made with thorotrast as well as other patients, and, what is more, one is easily able to make stereoscopic films during the same injection, which may be prolonged.

For these reasons I prefer thorotrast<sup>2</sup> to solutions of iodide for use in cerebral angiography, and I believe that it is the substance of choice for this procedure.

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2. Chemische Fabrik von Heyden Aktiengesellschaft, Dresden.

## Clinical Notes

### FAMILIAL PALLIDAL DISEASE WITH UNUSUAL FEATURES IN NEGROES

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Many familial extrapyramidal syndromes have been described in the literature. Outstanding are: the pseudosclerosis group, described by Wilson, Vogt's disease and Hallervorden-Spatz' disease.

It is known that there is a familial and hereditary element in Wilson's disease. The familial aspect has been studied by Rausch and Schilder,<sup>1</sup> who observed two sisters with the condition, and recently by Curran,<sup>2</sup> who observed a family, with consanguinity of the parents, in which all of the five children showed signs of pseudosclerosis. The hereditary aspect has been studied carefully by Kehrer.<sup>3</sup>

Vogt's disease, also known as status marmoratus, was first described by C. and O. Vogt. This disease is not so well known, and a short description will not be amiss. It is a disease in which there are spastic states and anomalies of posture of extrapyramidal character, with involuntary movements of choreic and especially of athetoid type. Associated movements, forced laughing and crying are observed. There is usually a tendency to improvement in the symptomatology. Sometimes the rigidity and sometimes the involuntary movements dominate the clinical picture. In some cases there are associated mental deficiency and epilepsy. Familial occurrence of the disease has been observed by Anton, Scholz and C. and O. Vogt. Oppenheim and C. Vogt observed a case in which it was hereditary. Hallervorden<sup>4</sup> discussed the question at length and gave a full bibliography.

Hallervorden and Spatz'<sup>5</sup> disease was described in 1922 as a familial disease of the extrapyramidal system. In this family the condition began in earliest childhood and was characterized by mental deterioration and by increased tonus to the point of the production of contractures. Similar cases have been described

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From the research department of the psychiatric department of Bellevue Hospital.

1. Rausch and Schilder: Zur Kenntnis der Pseudosclerose, Deutsche Ztschr. f. Nervenhe. **52**:414, 1914.

2. Curran: Pseudosclerosis of Strümpell-Westphal in Five Members of a Family, J. Neurol. & Psychopath. **48**:320, 1932.

3. Kehrer, F.: Ueber Erblichkeit und Nervenleiden, Berlin, Julius Springer, 1927; Psychiat.-neurol. Wchnschr. **29**:185, 1927.

4. Hallervorden: Die Anatomie der Psychosen, in v. Bumke: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1931, vol. 11, p. 1045.

5. Hallervorden and Spatz: Eigenartige Erkrankung im extrapyramidalen System mit besonderer Beteiligung des Globus pallidus und der Substantia nigra, Ztschr. f. d. ges. Neurol. u. Psychiat. **79**:41, 1922.

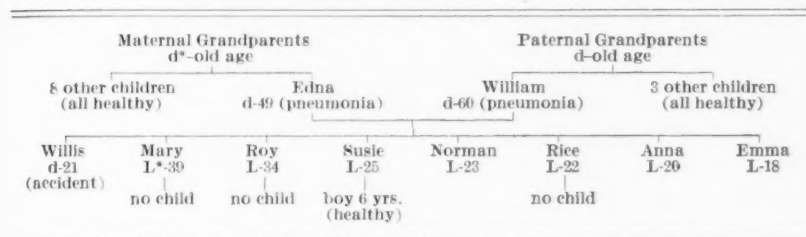
by Dercum,<sup>6</sup> in 1924, and by Kalinowsky,<sup>7</sup> in 1927. In 1932, Winkelman<sup>8</sup> reported an intensive pathologic study in one of Dercum's cases and reviewed the literature. Briefly, the pathologic process was limited to the pallidum and pars reticularis of the substantia nigra; the striatum (putamen and caudatum) showed absolute integrity. This was so outstanding that Winkelman was led to call the condition progressive pallidal degeneration.

Our cases conform closely to the clinical picture of the Hallervorden-Spatz group. Three of eight children in a family are affected. It was not possible for us to examine all the members of the family, but we were able to obtain a history from an older sister who is reliable and intelligent, and who assured us that no other members of the family suffer from the disease.

#### REPORT OF CASES

The general history, as obtained from an older sister (Mary), is as follows: There is no evidence of dwarfism or nervous troubles in the family, and the parents are not consanguineous.

#### *The Family Tree*



\* L means living; d, dead.

Norman, Anna and Emma suffered from the pallidal disease which we shall describe.

N. S. had a normal birth, with no difficulties in respiration or sucking. He was a very small baby. He talked at the age of 1½ years and walked at the age of 2 years. He seemed to be a normal child and entered school at 6 years. At the age of 7 a stooping posture and difficulty in gait were noticed. He walked on his toes. Next he began to be awkward with his hands. Later he began to have difficulty in talking. He has never had fits or any serious illness. There is no history of sleeping sickness or influenza. He attended school for three years. By the age of 10 or 11 the condition was fully developed.

E. S. and A. L. S. were of normal size at birth. Each had an uneventful infancy. At about the age of 10 years, there began difficulties similar to those observed in N. S. The disability began in the feet and progressed upward. Menstruation began at a normal age and is regular at the time of this report.

CASE 1.—N. S., a colored man, aged 23, is underdeveloped. The stature is that of a boy aged 10 or 11 (height, 140 cm.). The general proportions are good.

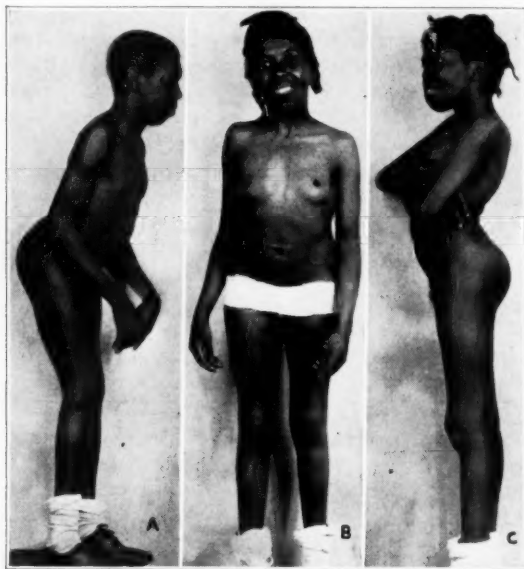
6. Dercum, F. X.: Two Cases of Retinitis Pigmentosa Occurring in Brothers, One Associated with a Spastic Symptom Group. *Arch. Neurol. & Psychiat.* **13**:651 (May) 1925.

7. Kalinowsky: Familiäre Erkrankung mit besonderer Beteiligung der Stammganglien, *Monatschr. f. Psychiat. u. Neurol.* **66**:168, 1927.

8. Winkelman, N. W.: Progressive Pallidal Degeneration, *Arch. Neurol. & Psychiat.* **27**:1 (Jan.) 1932.

There are bony deformities as evidenced by marked lumbodorsal lordosis and some bony hindrance to complete extension at the elbow joints. The skin is dry and scaly. The external genitals are well developed, and the distribution of hair is typically masculine. The teeth are well shaped and show no stigmas of congenital syphilis.

The posture is distinctive. The patient stands bent forward, with adducted arms and semiflexed elbows; the toes are turned in, and the abdomen is protuberant (fig., *A*). When he walks he adducts both legs and takes very irregular large steps; there are no associated movements of the upper extremities. He has a rather marked lack of impulse. There is no ataxia, and the Romberg sign is negative.



*A*, photograph of N. S., showing posture. *B*, photograph of E. S., showing typical facial expression. *C*, photograph of A. L. S., showing posture and facies.

There is marked generalized rigidity, extrapyramidal in type (plastic tone), which increases during several passive movements. This rigidity also involves the jaw and neck. The tone is stronger in the lower extremities than in the upper. All diadokokinetic movements are very slow, seemingly being hindered by tensions. There is a marked flexion combine. The legs have a tendency to go into rigid extension, with spontaneous Babinski phenomena on both sides (a rhythmic fanning of the toes with persistent extension of the big toes). After various passive movements, the rigidity becomes so intense that it cannot be overcome. The left hand at times goes into athetoid postures. In the finger-to-nose test there is hyperextension of the index finger but no tremor. There is general weakness in all the muscles but no real paralysis. The patient has a fair grip, and the power in the lower extremities is comparatively good. Speech is slurred and almost impossible to understand. He exhibits forced laughing which is not natural but is tonic, and perseverates for a while.

All the deep reflexes are active, except that ankle jerks cannot be obtained on account of tensions. There are no clonus or Babinski, Hoffmann, Rossolimo or Oppenheim reflexes. The abdominal reflexes are active.

There are no sensory disturbances.

The eyes deserve special mention, because they exhibit peculiar phenomena. The pupils react to light and in accommodation, but the reactions to light are changeable. When pressure of the hand is exerted by the patient, the pupils become wider and fixed to light. The fundi are normal. Examination with a corneal microscope shows a brownish-green pigment in the corneal margins; it is not typical of a Fleischer ring. There is no nystagmus. The corneal reflexes are equal and active.

Wassermann tests of the blood and spinal fluid were negative.

Roentgen examination revealed a small sella turcica; the other bones are normal.

Liver function tests (including the icteric index and the van den Bergh and the bromsulphthalein tests) gave normal results.

Mentally, the patient is an idiot. He can hardly talk, and can do little for himself. He exhibits marked akinesia and a tendency to forced laughing and crying. Usually his mood is indifferent or somewhat euphoric. His facial expression is tonic, and he tends to persevere.

The findings in the two other cases are almost similar.

CASE 2.—E. S., a colored girl, aged 18, is underdeveloped and undersized (height, 136.2 cm.), but has a well proportioned skeleton. She has marked lumbo-dorsal lordosis and a bony hindrance to complete extension at the elbow joints. The distribution of hair is typically feminine, but somewhat scanty in the axillae. The breasts are underdeveloped. The teeth are regular and bear no syphilitic stigmas. The patient walks stiffly, with a tendency to adduction and without any associated movements. The toes are turned in, and the feet are dragged somewhat. The Romberg sign is negative.

The pupils are equal and regular. The reaction is incomplete to light but it is good in accommodation. However, these reactions are variable, fluctuating within short periods. At times the pupils react promptly to light and at other times not at all. There is no nystagmus. The corneal reflexes are normal. The ocular movements are normal. There is a brownish-gray ring of pigment at the margin of the cornea where it meets the conjunctiva; when examined with the corneal microscope it is seen to be superficial and not a Fleischer ring.<sup>9</sup>

Examination of other cranial nerves gave negative results.

The speech is somewhat explosive, staccato and nasal. There are also forced laughing and the peculiar continuous smile characteristic of this condition (fig. B). The reflexes are active and equal on the two sides; there is a bilateral Hoffmann but no Babinski or Rossolimo sign. Sensory examination gave negative results.

This patient also has marked generalized extrapyramidal rigidity, though it is not so marked as that in her brother. She has hypertonia in the arms. Both legs are kept in extension and adduction. The feet are extended and supinated. She also shows plastic tone. Active movements are checked by the rigidity; otherwise they are normal. There is no atrophy, palsy, hypertrophy or involuntary movements. However, there is marked adiadosokinesis, especially on the left.

The reaction of the outstretched hands to turning of the head is marked. When the head is turned to the left, the left arm tends to move inward and has a paradoxical reaction. When the head is turned to the right, the tendency to adduction of the left arm is increased very much. There is an increased tendency of the trunk to turn in the direction of the head.

9. According to our observations this pigment is very common in Negroes.

Body measurements show a general restriction, with no disproportion. Tests of liver function gave normal results. The Wassermann tests of the blood and spinal fluid gave normal results.

Mentally the patient is an imbecile. She made a score of 38, at the 14 year level, on the Stanford-Binet scales. She shows hypokinesia. She will sit in a corner all day, doing nothing, but continuously smiling in a tonic way. When approached she becomes friendly, smiles and becomes playful.

CASE 3.—A. L. S., a colored woman, aged 20, is somewhat better developed than her sister, and the lordosis is not so marked. She also has a bony hindrance to complete extension of the arm at the elbow joints. The distribution of hair is normal. She, too, is undersized. The Romberg sign is negative. The pupils are equal and regular and react promptly to light and in accommodation. They do not show the variability of reaction which is characteristic in the other two cases. The corneal reflexes are normal. Movements of the eyeballs are normal. The patient also has pigment at the corneconjunctival junction, but microscopic examination of the cornea showed that it is not a Fleischer ring.

Speech is of the bulbar type. Forced laughing and crying and the tonic continuous smile are seen in this case also (fig. C).

The reflexes are equal and active. There is no Babinski or Hoffmann sign. Sensation is normal. This patient shows the same generalized rigidity that is present in the other two cases. She walks with extension and adduction of the legs, but without associated movements. The tensions are continually changing, so that active movements are checked. The patient has a continuous fanning of the toes and dorsal extension of the great toes, producing an attitude of pseudo-Babinski sign. There is no marked diminution in power.

Body measurements show a symmetrical constriction in all diameters. The height is 141.2 cm.

Tests of liver function gave normal results. The Wassermann tests of the blood and spinal fluid gave normal results.

Mentally, the patient can be classified as an idiot. Her score was 19 on the Pintner-Patterson performance test. She has the tonic smile and laughing that the other patients show and likewise the marked akinesia. She, too, is very playful and cooperative when approached.

#### COMMENT

The picture of the disease in all the cases is essentially identical. The condition began about early school age with progressive rigidity, starting in the legs. There is a tendency to athetoid movements. In all the cases there are a particular type of forced laughing and serious pseudobulbar disturbances in speech. Only in case 2 is a Hoffmann sign present. Profound mental deterioration with emotional disturbances is present in all the cases. Two cases (cases 1 and 2) show pupillary reactions to light which are akin to catatonic pupillary phenomena.<sup>10</sup> All the patients show marked dwarfism (the healthy sister showed normal growth), extreme lordosis and bony anomalies in the elbow joints.

Since there are no disturbances in the function of the liver and no typical Fleischer ring, a diagnosis of pseudosclerosis can be discarded. It is more difficult, however, to make a differentiation between Vogt's disease and Hallervorden-Spatz' disease. But the familial factor seemingly plays less part in Vogt's disease, and the clinical picture is not so much dominated by rigidities. In addition, there is

10. Schilder, Paul, and Parker, Sam: Pupillary Disturbances in Schizophrenic Negroes, *Arch. Neurol. & Psychiat.* **25**:838 (April) 1931.

a general consensus that Vogt's disease is not progressive—the condition is either the result of developmental disturbance or an early stage of encephalitis. In our cases, as in the cases of Hallervorden and Spatz, the disease started in childhood and progressed.

The picture, then, in our cases fits completely into that of Hallervorden-Spatz' disease. Rigidities are the outstanding characteristic in these cases. They are in relation to a lesion in the pallidum and the reticular portion of the substantia nigra. The onset of the rigidity in the lower extremities is rather common.

Cases of familial extrapyramidal disease in colored people have not been reported so far, and our observations merit interest from this point of view. Another point of interest is the dwarfism in these cases, which was not present in any other familial extrapyramidal syndrome reported.

The pupillary disturbances observed in two of our cases deserve further comment. They were notably changeable, disappearing almost completely in the later course of our observation. They were increased by muscular exertion and also by pressure on the iliac point and showed, therefore, the characteristics of pupillary disturbances that Westphal<sup>11</sup> and Meyer<sup>12</sup> have observed in catatonia, and Westphal<sup>13</sup> in many kinds of extrapyramidal diseases. It is possible that Negroes show pupillary changes of that kind more easily than do white people.<sup>9</sup> Westphal was of the opinion that the phenomena observed by him were due to striopallidal lesions. It is remarkable, at least, that one finds the pupillary disturbances in cases which are probably due to pallidal degeneration.

#### SUMMARY

Familial extrapyramidal syndromes are briefly discussed. Three cases of Hallervorden-Spatz' disease in a Negro family are described, with characteristic rigidity and akinesia and with severe mental and emotional changes. Unusual features, such as dwarfism, which were present in all of the cases, and pupillary disturbances, which were present in two cases, are reported.

11. Westphal: Ueber ein im katatonischen Stupor beobachtetes Pupillenphänomen, *Deutsche med. Wchnschr.* **33**:1080, 1907; Ueber Pupillenphänomene bei Katatonie, *Monatschr. f. Psychiat. u. Neurol.* **47**:187, 1921.

12. Meyer: Die körperlichen Erscheinungen bei Dementia praecox, *Allg. Ztschr. f. Psychiat.* **66**:866, 1909.

13. Westphal: Ueber Pupillen bei Encephalitis epidemica, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **68**:226, 1921; Zur Frage des von mir beschriebenen Pupillenphänomens bei Postencephalitis (Spasmus mobilis), *Deutsche med. Wchnschr.* **51**: 2101, 1925.

## CAVERNOUS HEMANGIOMA OF THE VERTEBRAE

E. M. HAMMES, M.D., ST. PAUL

In 1903, Muthmann<sup>1</sup> reported the first case of cavernous hemangioma of the vertebrae with a compression syndrome of the spinal cord. Since then reports of twenty-nine cases have been published, in fourteen of which there were clinical symptoms; in thirteen of these a compression syndrome of the spinal cord was noted. Sixteen cases were found post mortem without any previous clinical manifestations. Bailey and Bucy<sup>2</sup> reported a case in 1929, with clinical recovery following surgical intervention. This was the second case in the literature in which operation was successful. The authors thoroughly reviewed the literature up to that time. In 1931, Younghanns<sup>3</sup> published the third case, which occurred in a man, aged 62; a correct preoperative diagnosis was made by means of the typical roentgenologic findings. A laminectomy at the level of the second and third dorsal vertebrae resulted in complete recovery from the compression myelitis. Sandahl<sup>4</sup> reported a similar case in 1931, with some clinical improvement following laminectomy. In 1930, Connell and Hay<sup>5</sup> published a case of compression of the spinal cord of eleven years' duration. Postmortem examination revealed a cavernous hemangioma of the sixth and seventh dorsal vertebrae. Our case is presented because it is the fourth case in which operation was successful, and because the roentgenologic studies of the vertebrae did not present the picture described by Bailey and Bucy and others as typical of the condition.

### REPORT OF A CASE

The patient had a hemangioma of the sixth and seventh dorsal vertebrae, with marked compression syndrome of the spinal cord; two laminectomies were performed, the interval between being six months. Complete recovery, except for a positive Babinski sign, resulted.

*History.*—A girl, aged 17, who was seen in consultation with Dr. Wallace Cole on March 6, 1925, had been admitted to the Gillette State Hospital for Crippled Children on Feb. 26, 1925. The family and personal histories were without significance. The patient had been perfectly well until August, 1924, when she noticed a tendency to hold her back rigid and complained of an occasional slight pain in the middorsal region of the spine. In spite of this, she continued with her usual athletic activities, such as tennis, basketball, hockey and skating, until Feb. 5, 1925. There had been no increase of the symptoms referable to the back,

1. Muthmann, A.: Ueber einen seltenen Fall von Gefässgeschwulst der Wirbelsäule, *Virchows Arch. f. path. Anat.* **172**:324, 1903.

2. Bailey, R., and Bucy, P.: Cavernous Hemangioma of the Vertebrae, *J. A. M. A.* **92**:1748 (May 25) 1929.

3. Younghanns, J.: Hämangiom des drei Brust-Wirbelkörpers mit Rückenmark Kompression, *Arch. f. klin. Chir.* **146**:321, 1932.

4. Sandahl, C.: *Acta chir. Scandinav.* **69**:63, 1931 (quoted from Younghanns' article<sup>3</sup>).

5. Connell, W. T., and Hay, W. D.: Cavernous Angioma of the Epidural Space with Compression of the Spinal Cord, *Canad. M. A. J.* **22**:75, 1930.

but at this time there developed a limp in the left leg. It felt heavy and tired easily. Soon afterward there developed numbness in the left foot, which gradually extended upward. The patient continued with school work until February 12. Three days later, the right leg became similarly affected, and within a few days she had difficulty in climbing stairs. On February 20, the legs would not support her, and she went to bed. The numbness gradually involved the leg, and within a few days extended up to the waist line. The legs gradually became spastic and could be straightened out only with assistance. Soon after that, urinary retention developed. On admission to the hospital, on February 26, the bladder was markedly distended, and she had to be catheterized. There were frequent involuntary twitchings of the lower extremities, but no pain.

*Examination.*—On March 6, 1925, there was evidence of a complete transverse lesion of the cord at the level of the tenth dorsal segment. The patient was well nourished and lay quietly in bed, with occasional coarse involuntary muscular twitchings of both lower extremities. The general physical condition was normal throughout. Neurologically, all cranial nerves were normal. Both upper extremities were normal. Both lower extremities were completely paralyzed, markedly spastic, somewhat edematous and slightly cyanotic. Both knee jerks were definitely increased, with bilateral patellar and ankle clonus and a positive Babinski sign. Passively, all joints were movable within normal limits. Flexion of the thighs on the abdomen produced some pain in the lower dorsal region. There was no evidence of atrophy or tenderness of the nerve trunks. Sensation in all forms was normal in the face, upper extremities and trunk to the level of the umbilicus. From here down over the trunk and both lower extremities, tactile, pain and thermal sense were definitely impaired. Deep muscle, position and vibratory sense were lost. The abdominal reflexes were absent on the right side and very sluggish on the left.

The spine presented no deformity. The neck was freely movable in all directions. There were some tenderness and muscular rigidity at the level of the sixth, seventh and eighth dorsal vertebrae. Roentgenologic examination of the entire spine, laterally and anteroposteriorly, revealed no pathologic condition. The bodies, spinous processes and laminae of all cervical, dorsal and lumbar vertebrae were of normal appearance and density, except the left side of the body of the sixth dorsal vertebra, which showed only a slight appearance of localized rarefaction. (These films were again studied after the operation, and again after reading Bailey and Bucy's article.) Further roentgenologic studies were made on March 20, 1932. Anteroposterior stereoscopic films and a lateral film showed absence of the spinous processes of the sixth, seventh and eighth dorsal vertebrae, together with their laminae. There was a small area of apparent rarefaction of the body of the sixth vertebra. The films otherwise gave negative results.

*Laboratory Findings:* The urine was normal. Examination of the blood showed: pressure, 110 systolic and 60 diastolic; hemoglobin, 84 per cent; red blood cells, 4,500,000; leukocytes, 8,900; differential count, normal; Pirquet and Schick tests, negative.

The spinal fluid from lumbar puncture was under moderately decreased pressure; there was no increase with the Queckenstedt test; 2 cc. was removed after five minutes. It was clear and xanthochromic, but did not coagulate on standing; there were 2 cells, a strongly positive globulin reaction, a negative Wassermann reaction, and a colloidal gold curve of 0011223332. No quantitative estimate was made of the protein.

Spinal fluid from cisternal puncture was under normal pressure, with a definite rise when the Queckenstedt test was made. The fluid was clear and of normal color; all tests gave negative results.

A diagnosis of compression myelitis of the tenth dorsal segment was made; the etiologic factor was undetermined.

*Operation.*—On March 28, Dr. Wallace Cole exposed subperiostially the spinous processes and laminae of the fifth, sixth, seventh and eighth dorsal vertebrae; the periosteum was thickened. Considerable bleeding was encountered and was difficult to control. The spinous processes and laminae of the sixth and seventh vertebrae were removed, exposing the dura. Bone in this area was soft and bled freely. Granulation tissue was encountered. The hemorrhage was severe, but was finally controlled with hot packs. Because of the great loss of blood and the poor condition of the patient, no further exploration was performed. The patient had a very stormy period for forty-eight hours, requiring hypodermoclysis and stimulation. Subsequent progress was uneventful.

During the following few months there was very little change in the neurologic picture, except that sensation and spasticity improved slightly, but the sensory level remained constant.

*Second Operation.*—Dr. Cole operated again on Oct. 3, 1925. His surgical notes were: On exposure of the spinal cord in the region of the old operation, a granulation tissue-like mass at the site of the previous operation, later diagnosed as hemangioma, was found encircling the cord and attached to, but apparently not involving, the dura, except at one point at about the level of the seventh or eighth dorsal vertebra. Here, in removing the tumor tissue and old scar tissue, the dura was apparently torn, and the cord seemed to be involved beneath it. There was pulsation at this point. On account of the severe hemorrhage and the poor condition of the patient, nothing further was done. Hypodermoclysis had to be given; the patient gradually improved, and surgical convalescence was uneventful.

By Dec. 14, 1925, there was a slight return of motion in the toes. The legs were still spastic, with bilateral patellar and ankle clonus and a positive Babinski sign. All forms of sensation were normal throughout. Bladder function was somewhat improved. On May 28, 1926, the patient began to take a few steps. The gait slowly returned to normal, except for some weakness of the right anterior tibial muscle group. By Nov. 11, 1926, she had made a complete recovery, except for bilateral ankle clonus and the Babinski sign. Since then she has been examined about once a year, and at present has recovered, except for a positive Babinski sign on the left, which has remained constant.

Dr. Margaret Warick submitted the following report on the specimen from the operation on March 28, 1925:

"The tumor of the vertebrae consists of a gray, friable mass which bleeds easily on ordinary manipulation. The piece is small, but spicules of bone are present throughout the mass. Microscopic section shows numerous spaces, all filled with blood. Between them are a small amount of connective tissue and small pieces of bone, which is being replaced by the tumor, which consists of blood vessels. From all appearances of the pieces of tissue, the condition is typical of a hemangioma which is involving the bone tissue."

The following report on the specimen from the operation was submitted on Oct. 3, 1925:

"The tumor of the vertebrae and meninges consists of small masses of soft, red tissue, in some of which are spicules of bone. Microscopic section shows in the

masses from the meninges only dense connective tissue in which are a few very large, thick-walled blood vessels and a few small thin-walled vessels. But the sections from the vertebrae show the bone to be practically replaced by a new growth consisting of great numbers of thin-walled blood vessels or sinuses. In the walls of these are numerous basic-staining, spindle-shaped cells which in some areas form a mass of tumor tissue and in others form the walls of the blood spaces. The tumor, therefore, seems to be located in the bone of the vertebrae, while the meninges show only chronic inflammation. Diagnosis: hemangioma of the vertebrae."

*Comment.*—Bailey and Bucy emphasized the importance of the roentgenologic findings in arriving at a correct preoperative diagnosis. They called attention to the fact that the picture of reduction in bone density between parallel vertical trabeculae which are increased in density is pathognomonic of angioma of the vertebrae. Our case did not present this. One must consider the possibility that the hemangiomatous process had not sufficiently involved the bodies of the vertebrae to produce this characteristic picture.

The benign character of this type of tumor is again demonstrated in our case. There has been no evidence of recurrence in the interval of over six years. The comparatively rapid development of the compression syndrome, with evidence of complete spinal block, was a somewhat unusual feature and suggested several diagnostic probabilities.

According to Younghanns,<sup>3</sup> the accidental postmortem finding of vertebral hemangioma is not infrequent. In a series of about 10,000 postmortem examinations at the Schmorl Institute, approximately 10 per cent gave some evidence of hemangioma of the vertebra. In not a single instance was there any evidence of a compression syndrome of the spinal cord, in spite of the fact that in several cases there was complete involvement of an entire vertebral body, with an extension of the tumor to the transverse processes and laminae.

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#### CORRECTION

In the article by Drs. Lathan A. Crandall and Arthur Weil, entitled, "Pathology of Central Nervous System in Diseases of the Liver: Experiments with Animals and Human Material," which appeared in the May issue (29:1066, 1933) the two parts of figure 1, on page 1069, were reversed when the halftone block was made; in other words, the upper portion of the picture should be labeled *B* and the lower portion, *A*.

## Abstracts from Current Literature

THE COLOR OF THE MACULA (FOVEA) CENTRALIS. J. W. NORDENSON, Upsala läkaref. förh. **36**:267 (May 22) 1931.

In a previous paper the author and T. Nordmark presented the results of an ophthalmologic investigation of the retina of the eye after death. This investigation was to determine whether a yellow color is always present in the macula of the eye after death. Former authors (as Schmidt-Rimpler) had assumed that such a color is always present in a living eye; but as long as the retina remains clear it is invisible, becoming apparent only at the darkening of the retina.

If this assumption is correct, it would be logical that any yellow color existing should become visible coincident with death. This was not their experience. It was only rarely that they found any yellow in the macular region of the eyes they examined. Usually the eyes were gray after darkening, without a trace of yellow. Nordenson presented certain autochrome photographs of eyes studied at various intervals after death. In these the macula was pure gray, whereas the fovea was red. No color was visible in the fovea or in the macular region. If such a color was always present, it would have appeared on these films, because one of them did show a yellow color in the macula.

In a discussion of a paper covering the ophthalmic picture of the fundus after death, Comberg criticized the author and his associates for not discussing the work of Vogt, who considered that he had established definitely the presence of macular pigment. Nordenson stated in reply that by the work in question he intended only to experiment with this problem by simple methods, and did not attempt a thorough investigation of the whole field. In order not to leave these comments wholly unanswered, Nordenson outlined his explanation as follows: "The main objection which could be raised about the ophthalmoscopic examination of the eye after death, from Vogt's point of view and reflections, is that his eyes were examined by ordinary daylight and not by red-free light, for by the use of this a yellow color would have been more easily seen. They used this ordinary light because they intended to investigate by a method which was practical for the ordinary eye physician, who does not have extensive laboratory equipment at his command, and secondly, to arrive at an independent conclusion of this problem, if possible. They felt that any yellow if present would have appeared with sufficient clarity even in this illumination. They, however, also made investigation of eyes after death by red-free light. When possible, a drop of 1 per cent atropine solution was instilled into the conjunctival culdesac before death, and the examination started immediately after death. In this way twenty eyes were observed, most of them immediately after death had occurred. In the majority of these eyes, the fovea appeared dark brown, surrounded by pure greenish-gray, dark retina in which there was no trace of yellow either in the macular region or in the periphery. They were also able to show this in pictures taken of the fundus in the red-free light on the autochromatic films. In some of these cases, one could see a clear yellow in the retina at the fovea and in its surroundings, which proves that yellow, if present, also shows in this illumination. In these cases, for the most part, a plica centralis had developed. In the cases with yellow macula, the fovea was a typical Leichenmakula fovea."

The conditions before examination by the red-free light, therefore, seem to be analogous to those made in ordinary light, and they give no basis for the assumption of pigment in the living retina which would become visible on its darkening. Further investigations were carried out to test several of the arguments already quoted to prove the presence of yellow in the eye. The eyes used for this examination were all normal, because the examination of a pathologic eye offers more difficulty in judging the results and carries less conviction.

A difference of opinion had existed between Gullstrand and Vogt. They wished to investigate this also. Gullstrand emphasized that the examination of eyes after death by daylight proves that there is no yellow in the macula lutea. Yellow, if present, should be visible when one is looking at the central spot of the macula. Since this little central spot is the thinnest place in the retina, a discussion of color appearance and intensity of light must be considered. It is certain that the light reflected by the retina is of one intensity, while that reflected from the deeper portions of the retina is below this same intensity. Therefore, the visibility of yellow pigment, if present, depends in part on the intensity of the light. Vogt answers this analysis of Gullstrand as follows: "I should consider this conclusion inevitable only if it were proved that a yellow color present (if there is any present) in a certain part of the retina would be visible by a light of a higher or different intensity than that for examining the surroundings of the dark spot. Such proof is not at hand."

Nordenson continues to say that if one lays a piece of dark gray photographic paper on a smaller piece of dark paper or cloth of a much deeper saturation, and then places over this a yellowish glass, this paper will appear gray even in moderate daylight, and the center will be black. One is not able to perceive the yellow of the glass, not even over the gray paper. The light which the latter reflects has passed over a threshold of visibility, but it is not strong enough to permit recognition of the yellow color in conjunction with the inner reflection of the glass. The latter becomes visible only in a light of a much higher intensity.

The objections of Vogt to Gullstrand's theory are logical and must be considered the more carefully since yellow light requires a fairly high intensity to pass over a visibility threshold. The vital point of this difference of opinion is, therefore, whether light which suffices to render visible the little dark spot in the fovea would be sufficient for recognition of the yellow color if it were yellow. Gullstrand is of the opinion that the light is sufficient. Vogt considers this unproved.

In order to judge this controversy, Nordenson carried out the following experiment: A subject was chosen who had a strongly pigmented fundus. In such an eye, first, much light is reflected from the pigment epithelium of the retina, and, secondly, some of the light is retained or absorbed by the choroid and portions of the retinas themselves. There were two conditions obtained from this experiment. First, in this eye Nordenson discovered, by approaching and receding the arc light (with the red-free light of Vogt), a certain optimum intensity of illumination wherein the little dark spot in the macula looked colorless, but neither in it nor in the surrounding retina was any yellow light (color) visible. This was thus a comparison of light intensities, considering that the light was reflected from the superficial retina as well as from the deeper portions of the retina. After this evidence was established, an artificial eye was placed before the ophthalmoscope at the same distance, i. e., in the same relationship of ophthalmoscope light and eye as was present with the subject. The fundus of the artificial eye consisted of a piece of dark photographic paper in the center of which was a hole closed with darker velvet, and a piece of film was superimposed, which had been freed of silver and then placed in a 1 per cent solution of trinitrophenol for one minute to dye the gelatin layer yellow. On examination of this artificial fundus by sufficiently strong light, the yellow color was clearly visible. It was then evident that the yellow color of the artificial eye was conspicuous in a light intensity which was insufficient for it to become apparent in the fundus of the patient's eye. Indeed, one could see this color in the artificial eye at double the distance from the light, a distance representing a diminution of three quarters of the light intensity.

A comparison was made with an enucleated human eye in which a typical post-mortem macula was present on examination. A yellow color was visible in this eye also, in a much weaker light intensity than was necessary to render visible the yellow color in the eye of the subject. From these repeated experiments, all with the same result, Nordenson concludes that the red-free light that is reflected

by the retina of an eye and that is of sufficient intensity to show as colorless the dark spot of the fovea would be sufficiently strong to show it as yellow were it yellow.

Another objection of Vogt's is that, if the yellow color in the macula proceeded from a membrane behind the retina, one would find the yellow color also in other parts of the fundus, and he states that he has found no other spot which produces the same yellow as the macula, or, indeed, any yellow at all. Nordenson thinks that this statement can hardly be proved—that no other spot in the fundus shows yellow.

Olsson demonstrated before the seventeenth meeting of the Swedish Ophthalmological Society that with the red-free light of Vogt one could see in the periphery of the fundus a very pretty yellow color. Indeed, in one instance, it was clearer there than in the macula. Nordenson has also been able to observe this in several eyes; i. e., the periphery presents the same yellow as the macula so far as it is possible to judge from the naked eye. He outlines a belt about the macular region as wide as the papilla itself which is greenish gray. This greenish-gray part might be coincident with the region of the retina that is thicker than the fovea itself. Therefore, as Nordenson states, "neither does this objection of Vogt seem to me to be justified."

Nordenson calls attention to an investigation of this subject by Koeppé, which he thinks is important. This investigator examined the fundus by means of a contact glass, using a slit-lamp microscope. By this he could investigate the structure of the fundus. By this method he found that by playing the beam of light from the slit-lamp over the retina, an illumination of the retina occurred which was similar to that seen in the cornea, when the beam of the slit-lamp passes over the cornea. He describes his observations as follows:

"The retina taken as a whole, as in this slit-lamp picture, has a distinct and easily perceived thickness, which seems to correspond to the apparent thickness of the cornea and is always distinctly perceptible; in indirect light, it is especially easily observed. One can also readily see how this thickness of the retina decreases regularly from the papilla to the beginning of the macular region.

"In the macula this slit-lamp illumination, which customarily appears as a light yellow red, becomes darker and, moreover, of a grayer red; i. e., the apparent optical thickness of the retina decreases quickly toward the fovea, without, however, lessening to a theoretical zero. In the fovea one can also still see that from the surface of the fovea and the pigment epithelium, there is a distinct thickness of the retina and that in the region of this layer the true foveal reflex in the focal light of the slit-lamps reveals the peculiarities mentioned above."

In this description it is interesting that Koeppé distinguishes the path of light outside the macula as lighter yellow red, whereas within the macula he states the light to be of a more grayish-red. This does not agree with the assumption of the presence of a yellow pigment in the retina, a view which Koeppé, by the way, supports in the study mentioned, for in cases of embolism of the central artery he observed, by the slit-lamp microscope a yellow patch around the fovea from which he apparently deduces a pigment to be present in life.

Nordenson performed this same experiment, using the red-free light of Vogt. He also saw the retina as a greenish gray and never as yellow. This experiment, therefore, seems to argue against a yellow color in the macular region of the retina present in life.

Nordenson then presents still another argument, although he says that it is of subordinate importance, for the granules of the fovea could be examined more easily by a simple central reflex free ophthalmoscope with red-free light. He finds in this, "that the granules seen with the Nernst slit-lamp are visible as dark granules on yellow pigment (using red-free light)." Since these granules could not possibly have been seen if no light had been reflected from the deeper portions of the retina, it is imperative, as Vogt also wrote, that the amount of reflection plays an important part. Vogt himself stated that "if one withdraws from the source of light (using divergent light) the yellow in the center of the retina disappears."

Nordenson states, therefore, that "we can hereby determine that the granulations are always visible when the yellow color is seen." Indeed, one can still see them after the yellow has disappeared in graded reduction of the light intensity. In the original paper, the following statement is in italics because of its importance: *It, therefore, follows that the yellow is seen only if the light in the center proceeding from the deeper parts is of a certain intensity after it passes through the retina. The opinion of Vogt, which agrees with this is, therefore, physically affirmed.*

Vogt, however, who seems to cherish some hesitation in regard to his earlier views, adds to this as follows: "Permit me to mention that the granules often appear to me lighter than their surroundings, not darker; that, further, in decreasing the intensity of the light I see the granules disappear first, and then the yellow." In this observation, the author states, "an error can easily be made because of its subtlety." He also performed the experiment, and it seemed to him that the yellow disappeared first, and then the granules. One must, therefore, agree with Vogt that this investigation is a delicate one. One cannot use it to draw any sure conclusions in regard to the question under discussion.

In concluding this paper the author states that, considering the facts mentioned, it seemed rather premature when Vogt stated, in his description of the examination of the eye by red-free light, that the question of yellow in the macula during life can be regarded as settled and in the affirmative. For such a conclusion, he (Nordenson) feels, the necessary proof does not yet exist.

SPAETH, Philadelphia.

THE LATE SYNDROME OF CONCUSSION IN CLOSED TRAUMATISMS OF THE SKULL.  
F. BREMER, H. COPPEZ, G. HICGUET and P. MARTIN, Rev. d'oto-neuro-ophth.  
10:161 (March) 1932.

This article is a report to the Sixth Congress of Oto-Neuro-Ophthalmology. The subject is considered under the following heads: Subjective and objective symptoms (clinical and radiologic), pathogenesis and therapy. The frequency of the syndrome varies, among different statistics, from 50 to 95 per cent. According to Alajouanine, Maisonneuve and Petit-Dutaillis, it is three times more common in patients with a lesion of only the external table than in those who have a cranio-cerebral wound. Too often these patients are regarded as psychopathic or as simulating the condition. The subjective symptoms are headache, giddiness, nervousness, insomnia, mental asthenia and dysmnnesia, and otologic and ophthalmologic disturbances. Headache is common, is usually diffuse or located in the frontal or occipital regions, is increased by change of position of the head, prolonged mental and physical effort and sensory stimuli. Vomiting is rare, which distinguishes the syndrome from hypertensive headaches and migraine. The headaches more commonly occur in the evening. Giddiness appears either as a sensation of a veil before the eyes or of a fog sprinkled with sparks or as staggering, although the patient rarely falls. It is distinguished from true vertigo, which is accompanied by a sensation of turning or lateropulsion, nausea and sweating, and also from larval epileptic manifestations, which are accompanied by a short period of unconsciousness, of which the patient has no recollection. Nervousness is represented by an exaggerated reactivity to various stimuli; that is, there are visual, auditory and olfactory sensory hypesthesia; or by a hypermotivity, expressed by choleric irritability, alternating with periods of depression. The symptoms are exaggerated by alcohol, even in small doses. Insomnia is always present, sometimes accompanied by diurnal somnia.

Mental asthenia and dysmnnesia are frequent. Concentration of attention is difficult, and there is lack of memory for the period following the accident and deficient memory for facts of recent date. After effort mental fatigue quickly ensues.

The ophthalmic symptoms are as follows: retinal asthenia that is not allied with accommodative and muscular asthenopia; concentric contraction of the visual

fields; amblyopia without lesions of the eyegrounds, which varies in degree from day to day, and retinal hypertensive symptoms. The otologic symptoms are tinnitus (relatively rare) on the side of the lesion and sometimes synchronous with the pulse; true vertigo, most often horizontal, which appears spontaneously or after effort and changes in the position of the head and is usually accompanied by headache and sometimes by nystagmus, nausea, pallor, sweating and vomiting.

In children there are important changes in disposition. They have frequent fits of anger, are cruel and are difficult to manage or to educate. In the aged the symptoms are much more intense, owing in part to an associated arteriosclerosis.

The description of the objective symptoms is based on fifty-seven personal cases seen during the past two years. There are no pathognomonic signs. Tachycardia occurs in one third of the cases; diffuse exaggeration of the tendon and palpebral reflexes, trembling, marked emaciation, spots of congestion on the face and hyperidrosis occur less frequently. Thermic instability has been noted by some observers and not by others. It is probably a focal symptom in cases with a lesion near the heat-regulating center.

Ophthalmic and otologic signs are described at length. Tonoscopic observations on the central artery of the retina in cases of concussion were described by Bailliart and Worms, who found hypertension to be frequent. In seventy per cent of thirty-six of the authors' cases, hypertension of the retinal artery was found, and there was no parallelism with the subjective symptoms. The flexibility of the arterial walls was not altered. The retinal arterial tension is not stable; hence, in evaluating this sign, precautions must be taken to avoid conditions that might influence it. Injections of distilled water intravenously or inhalations of amyl nitrite increase the tension temporarily. There is a loose relation between amblyopia and the arterial tension; in seven of ten cases with amblyopia, the tension was above 50. There is not a close relation between the tension and the extent of contraction of the visual fields. The relation between the intracranial tension and retinal arterial tension in cases of concussion of some duration is not close. Serra found the proportion to be 9 per cent of the former to 55 per cent of the latter. In cases of pure concussion, true papillary stasis was not found.

Measurement of the retinal venous tension may furnish information of the pathogenesis of concussion. It is important to note whether, on applying the dynamometer, the vein is overwhelmed at once (hypotonia) or whether pulsation precedes the obliteration (hypertonia). Perhaps this procedure may permit a prejudgment of the efficacy of a proposed decompression; if the tension is at or below normal, a cephalospinal hypertension can hardly be the basis of the syndrome.

In five cases pupillary changes were found; there were inequality in two, slow reactions in two and double mydriasis in one. The sign of Argyll Robertson has not yet been demonstrated. Disturbances of coordination of associated movements of the eye, described by Mann, are probably focal signs.

The otologic signs are important when taken altogether, for they permit a conclusion with regard to simulation. The sign of Muller (dilatation of the vessels of the epitympanum) is of value when it confirms other manifestations of encephalic hyperemia. When the functional examination of the cochlea yields discordant results, examination of the cochlea reflex (cochleopalpebral, cochleopupillary) will determine whether the patient can hear. Diminution of hearing for the watch may coexist with normal hearing for the spoken voice. It accords with the diminution of bone perception and the shortening of perception of the high and middle tones by air. Lowering of the upper tone limit may be the only auditory sign, but it often coincides with inexcitability of the vertical semi-circular canals. The spontaneous vestibular signs, Romberg's, Babinski-Weill's and pastpointing, must be clearly positive and must agree with each other to be of value. Spontaneous nystagmus is rare. When its direction is toward the hypoexcitable labyrinth, a central lesion is indicated. Rhese believes that it occurs especially when one of the labyrinths is hypo-excitable and is a phenomenon of

decompensation, dependent on vasomotor disturbances. Instrumental tests of the labyrinth often provoke or augment the headache, determine epileptic crises and are followed by tachycardia. Rotation usually produces a nystagmus of lessened duration; sometimes it is accompanied by intense reactive phenomena, while the caloric reactions are normal or subnormal. Caloric tests were made after the technic of Brunings; injection of 75 cc. of water at a temperature of 27 C. and measuring the duration of the resulting nystagmus. In position I, the two sides rarely reacted alike. In nine cases no reaction was obtained, even after the use of 250 cc. Bouchet was struck by the frequency of lack of reaction from the vertical canals and the great resistance to the galvanic current in such cases. In Bouchet's forty-eight cases, there was a prompt reaction to the galvanic current in thirty-nine. In only three cases was there a distinct bilateral hyperexcitability. The galvanic test is useful in revealing a bilateral or unilateral hypo-excitability for falling or nystagmus.

When hyperreflectivity of the vestibular apparatus exists, it is unilateral. It usually means a recent trauma or a central lesion. If the former, compensation usually takes place within a year if the condition is of labyrinthine origin. If the phenomenon persists for more than two years, it points to a central lesion. Hypo-excitability is most frequent, and often there is dissociation; the rotatory reaction is the less often diminished. At times all the vertical and horizontal canals are hypo-excitable.

It is only since the World War that detailed studies of the cerebrospinal fluid in cases of cranial traumatism have been made. The pressure is apt to be increased, though in a minority of cases it is lessened. Arnaud and Crémieux found alternation of high and low pressures, caused by spasm of the intracranial vessels. Qualitative alterations in the fluid are rare in old cases and when present are not pathognomonic. Encephalography yields important information. Stereoscopic plates, made in different positions, are necessary. The method reveals: (1) absence of filling of the ventricles, indicating obstruction in the channels of fluid; (2) increase in volume of both lateral ventricles or deformity of the ventricle on the side of the lesion; (3) accumulation of air in the subarachnoid spaces of the base or convexity. Too much reliance must not be put on the observations when they are not supported by clinical evidence. The method is without danger in traumatic cases and is of value in doubtful cases.

Anatomopathologic data in the pure late concussive syndrome are rare. Autopsies were made in two cases of Haase's and three of Rosenhagen's. The observations were: (1) microscopic foci of cerebral contusion; (2) craniomeningocerebral adhesions, with subjacent areas of softening; (3) disseminated microscopic perivascular lesions with softening, resulting from hemorrhage; diffuse or perifocal degenerative reactions, either ganglionic or neuroglial, apparently progressive. Latterly, much experimental work has been done. Mairet and Durante studied the effect of the discharge of explosives on animals and found: 1. Large numbers of small tuberosities projected from the surface of the cortex (small necrotic cortical zones). 2. There was vacuolation in the layer of Bechterew and in that of the motor cells, accompanied by diffuse nuclear proliferation; the motor cells were atrophied. 3. The motor cells were disposed in columns; this is the result of the destruction of certain radial capillaries, the cells nourished by them having disappeared. 4. At certain points, there were trains of sclerosed neuroglia, which did not extend beyond the gray substance. 5. More rarely microscopic splinters of the internal table determined a reaction of fusiform cells. Penfield found that a minimal lesion produced a long-lasting phagocytosis, and that transplantation of any tissue on the surface of the brain is followed by rapid proliferation of fibroblasts above and below the graft. Cranial traumas lead to the formation of connectivogial cicatrices which remain active for a long time, and which cause deformity of the brain and ventricles and produce remote effects.

The parts of the auditory apparatus more often injured are the nerve and its branches; this is followed by atrophy, due to hemorrhage. Osseous lesions are less frequent.

The pathogenesis of acute concussion must be distinguished from that of the late syndrome. The explanation of the fact that the late syndrome is more frequent in cases of closed trauma is that when there is an osseous break, the shock to the brain is much less. There is frequently a latent period following the acute phase, which is followed by an aggravation of the symptoms. The latter is caused by the process of repair, but the mental reaction of the patient to his condition and to the question of claims for damages has an influence. The mechanism of the production of the headaches may be adhesions between the cortex and the meninges, vasomotor disturbances or alterations in pressure and distribution of the cerebrospinal fluid. Dizziness may be explained by congestive vasomotor disturbances. Cerebral hyperemia is indicated by hypertension of the central artery of the retina; if that condition is present, there is likewise cerebral arterial hypertension. Compression of the brain excites special vasomotor centers. Tournade has demonstrated that the cerebral centers contain a circulatory-regulating apparatus, and that hypotension or hypertension in the brain determines cardiac and vascular reactions that regulate the blood pressure. An increase of retinal tension is observed much oftener than hypertension of the cerebrospinal fluid. The laws governing the cerebral and retinal circulations are quite different from those dominating the general circulation. The cerebral vessels are little sensitive to vasomotor stimuli of the sympathetic or to such vasoconstrictors as epinephrine. The microscopic traumas in the brain exercise a continuous but varying irritative action on the cerebral vessels, which accounts for the fluctuation in the symptoms. The results of tonoscopy tend to show that disturbance of the cerebral circulation is the basis of the concussive syndrome.

The disturbances of the internal ear are due to destructive lesions from hemorrhages in pathways of the vestibular and cochlear nerves. These lesions become more apparent under the influence of vascular disturbances, sequels of traumatism, which bring to light the labyrinthine disequilibrium.

The nervousness, mental asthenia and dysmnnesia and other psychic symptoms are directly dependent on organic cerebral changes, but are modified by the underlying terrain (nervous constitution).

Well conducted treatment in the acute stage of the condition will cure many patients. This consists of rest in bed for at least three or four weeks, frequent saline purges, repeated lumbar punctures until the fluid becomes normal and the administration of methenamine when there is leakage of cerebrospinal fluid from the nose or ear. In the late stage, rest, general hygiene and prolonged sedative medication, such as sodium bromide with peptone, a combination of bromides, papaverine and phenobarbital, and analgesics as needed are required. If there is hypertension or hypotension of the cerebral fluid, intravenous or rectal injections of a hypertonic solution or intravenous injections of distilled water, respectively, are indicated. The injection of from 40 to 95 cc. of air into the subdural space is warmly recommended. The air should be introduced slowly, with the patient recumbent and the head slightly elevated. Five cubic centimeters are injected at a time, and more fluid is withdrawn than air put in. In certain cases in which there are focal lesions, surgical intervention is required.

The prognosis is rather unfavorable. Relapses may occur, even in light cases. Only after at least three years should stabilization be expected. The degree of incapacity of these patients should be carefully estimated. For cases of the first degree, it will amount to from 40 to 50 per cent; for those of the second degree to from 80 to 100 per cent.

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PROBLEMS IN LEFT-HANDEDNESS, WITH INVESTIGATIONS ON STUTTGART CHILDREN. MARIA SCHILLER, *Ztschr. f. d. ges. Neurol. u. Psych.* **140**:496 (July) 1932.

There has been no extensive study of left-handedness since Stier's fundamental monograph in 1911. He found an average of 4.6 per cent of left-handedness among soldiers. Inman and Ballin found 2.85 per cent in America, and Kapustin reported

3.8 per cent in Russia. Schott-Esslinger found 11.49 per cent of left-handedness, a figure which does not compare with the 4.06 per cent found by Schafer in a study of Berlin school children. Statistics seem to show that left-handedness increases from east to west, and that it is present in varying degrees. Stier believed that the Latin races show a greater tendency to left-handedness, and other authors assume that it is more frequent in countries with a high consumption of alcohol. Left-handedness is more frequent in men than in women. Stier's figures were 3.6 per cent for men and 2.1 per cent for women. Schafer found 5.1 per cent of boys with this trait and 2.9 per cent of girls among his Berlin school children. Schott found 14.1 per cent boys and 9.1 per cent girls; among adults, 12.7 per cent men and 9.4 per cent women.

The hereditary factor in left-handedness is a moot point. There are two widely divergent views, represented by Stier and Bethe. Stier maintained that every left-handed person comes of left-handed forebears, and that inheritance follows strictly mendelian lines. Bethe believed that exogenous influences are more important than inherited tendencies, and he stated that 90 per cent of left-handed people could be changed to right-handed people in early youth. Stier believed that left-handedness is 100 per cent inherited; Schafer gave the percentage of inheritance as 60, and Schott, as 47. Redlich believed that a relatively large percentage of mental and nervous patients are left-handed. Rosenfeld commented on the frequent coincidence of difficulty in understanding and disturbances of speech in ambidextrous and left-handed persons. Schott found 12.7 per cent left-handed persons in institutions for the feeble-minded; in one institution of severely feeble-minded people, he found that 17.5 per cent were left-handed. Steiner and Heilig found 89.5 per cent left-handed people in epileptic families. Redlich believed that 21.9 per cent of epileptic people are left-handed. Lombroso first called attention to the high incidence of left-handedness among criminals. The percentage varies from 11.2 to 22.2 per cent.

The relation of left-handedness to disturbances of speech has often been commented on. Steiner and Heilig pointed out the triad of left-handedness, epilepsy and stuttering. Kistler found stammering often in left-handed people, but not stuttering. Inman and Sachs commented on the combination of left-handedness and stuttering. Inman asserted that almost all who stutter are left-handed. Sachs pointed out the occurrence of stuttering in soldiers who had lost their right arms and were forced to use the left. Scripture reported similar cases; likewise, Orton asserted that changing from left-handedness to right-handedness furthers the incidence of stuttering. Subert and Kapustin found left-handedness in 8 per cent of stutterers. Stier found that 13.5 per cent of left-handed soldiers showed disturbances in speech, and that 8.5 per cent stuttered. He also called attention to the frequency of stuttering in left-handed families. There are total, partial and latent left-handed people. There are left-handed people who are also left-footed and left-eyed. There are also left-handed people who are right-footed and right-eyed, and there are right-handed people who are right-footed. Many combinations are possible.

Schiller investigated 10,108 children in Stuttgart schools in 1930. There were 3,917 boys and 6,191 girls. In 1931, she studied 7,651 children, of whom 2,520 were boys and 5,131 were girls. She classified as left-handed children who used the left hand preferably in work such as drawing, handwork, sewing, throwing a ball, chopping wood and cutting bread. She also called left-handed children who were right-handed but were obviously left-footed.

Of 7,651 children of the period of 1931, 594 or 7.77 per cent were found to be left-handed in the stricter sense, and 95 or 1.24 per cent in the wider sense, as already indicated. Of these, 10.08 per cent were boys, and 6.63 per cent were girls. Of 594 left-handed children in the stricter sense, the families were left-handed in 329 or 54.76 per cent. Of 95 left-handed people in the wider sense, 15 families were left-handed, or 14.56 per cent. Among 254 strictly left-handed boys, there were left-handed families in 128, or 50.39 per cent; of 35 left-handed boys, not strictly left-handed, 6 were from left-handed families, or 15.79 per cent. Of 340 girls who were left-handed, 201 were from left-handed families, or 59.12 per cent; of 60 who were left-handed in the wider sense, 8 families or 13.33 per cent were left-handed.

Schiller studied the relation of the type of school to the inheritance of left-handedness, but only in a group of girls. She found left-handedness inherited in 52 per cent of left-handedness in public schools, in 68 per cent in higher schools and in 80 per cent in gymnasia. She is unable to explain the high figures in the latter. These children come from the intellectual circles and are better observed.

Schiller investigated also the degree of left-sidedness. She tried to determine how many left-handed people are also left-footed. Of 254 left-handed boys, 122, or 48.07 per cent, were left-footed. Of 340 left-handed girls, 193, or 56.76 per cent, were left-footed. Of these 594 children, 315 were left-footed, an average of 52.42 per cent. How many of these left-sided persons inherit their tendencies? Schiller says 62.34 per cent, whereas in left-handed and right-footed persons only 32.72 per cent have inherited the trait (22.72 per cent boys and 42.72 per cent girls).

Eyedness was studied in older school children. Of 399 girls, 42 were left-handed and 89 or 22.3 per cent were left-eyed. Of the 89 left-eyed children, 20, or 22.47 per cent, were left-handed and 69, or 77.6 per cent, were right-handed. Of the 42 left-handed children, 20, or 47.6 per cent, were left-eyed. Of the 20 left-handed, left-eyed children, 15 were also left-footed. Of these 15, 13 came from left-handed families. The other 5 were right-footed, and 3 came from left-handed families. Of 103 boys, 12 or 11.6 per cent were left-handed, and 24 or 23.3 per cent were left-eyed. Of 24 left-eyed boys, 6 or 25 per cent were left-handed, and 18 or 75 per cent were right-handed. Of the 12 left-handed boys, 6 were left-eyed. Schiller concludes that left-handedness predisposes to left-eyedness more than does right-handedness. About one half of all left-handed people are left-eyed, and left-eyedness is most frequent in total or familial left-handed persons.

The relation of left-handedness to disturbances of speech was studied in the Stuttgart schools. Of 2,520 boys, 41 stuttered, and of these 7 were totally left-handed; left-eyed and left-footed. There were 34 right-handed stutterers. Of these 8 were probably left-handed, 4 were left-eyed and came from left-handed families; 1 was left-footed and came from a left-handed family; 1 was left-eyed and from a right-handed family; 1 was right-footed and right-eyed, and from a right-handed family, and none was right-footed. Schiller believes that among stutterers there is a greater percentage of left-handed people than among normal people. Of 5,130 girls, 20 stuttered. Only 1 was left-handed. There were 19 right-handed stutterers.

Schiller made some observations on children in the lowest grades and found 1 left-handed girl of 222 with disturbance of speech and 17 left-handed boys of 305 boys, of whom 11 were stammerers and 6 stutterers; 3 were left-handed, and 3 right-handed. Six of the stammerers were left-handed.

Schiller stated that mirror writing is one of the classic symptoms of left-handedness, and that one finds it practically always, though in differing degrees. It is also a symptom of latent left-handedness. Of 345 left-handed people, Schiller found only 10 who could not do mirror writing.

Left-handed people should not be forced to change their mode of writing.

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SCIENTIFIC STUDIES AND PERSONAL OPINION ON SEX QUESTIONS. GOODWIN WATSON and GERALDINE GREEN, *J. Abnorm. & Social Psychol.* **27**:130 (July-Sept.) 1932.

Just what is the worth of scientific investigation on social and sexual subjects is asked by Watson and Green of Teachers College, Columbia University. Is it true that such an investigation discloses either facts that are wrong or ones the truth of which is obvious to the average educated person, as has been frequently alleged, assuming that the graduate students of an eastern college are acceptable as representing such a class? A questionnaire was given to graduate students requesting them to record their preconceived opinions (guesses) on forty-five social and sexual questions. The answers were to be compared with the findings of

Hamilton and Davis who compiled research data on the same topics as those on which the students were asked their opinion (Hamilton, G. V.: "A Research in Marriage," New York, Albert & Charles Boni, 1928 and Davis, Katharine B.: "The Sex Life of 2,200 Women," New York, Harper & Brothers, 1929, p. 20). In this way a determination could at least be made as to just how "obvious" were the research conclusions. A strictly nonpartisan attitude is assumed in this matching of general opinion (as represented by the graduate class) against the records of the research. Without comment the students' opinions and guesses are compared with the research findings of Hamilton and Davis.

Fourteen of the forty-five questions disclosed such a wide divergence of opinions among the students on the topics in question that unmistakable general opinion trends could not be deduced. These are not properly utilizable for positive comparison with "existing" evidence. There was, however, a substantial public opinion among the students prepared to agree with such statements as: Men have more chance than women for marital happiness; most husbands are older than their wives; disposition, temperament and character are fundamental in marital success; men tend to choose their mothers as preferred parent; women their father; money matters are more troublesome to women's marital happiness than to men's; most people believe that they and not their lovers ended the affair; the more highly educated partner is more apt to be dissatisfied; regular intercourse experiences contribute to working efficiency; unusually frequent intercourse during the first year of marriage tends to go with marital unhappiness; psychoneuroses are more common among the sexually inadequate; a traumatic sex experience in childhood interferes with normal sex development; women tend to be more critical of husbands than men of wives; men with sisters and girls with brothers are more apt to work out happy marriages; the average college woman marries at about the age of 26, men at about 30; having had some experience of masturbation brings no serious detrimental influence on health or chances for marital happiness; about 25 per cent of college girls have had overt homosexual experiences; for women to have had a "crush" with overt homosexual expression exercises no seriously detrimental influence on health or chances for marital happiness; women's colleges graduate a larger proportion of girls with homosexual experiences than do co-educational schools; ninety per cent of college graduates approve of making birth control information available to all married couples; about half of modern marriages work out happily; about 15 per cent of married persons are seriously dissatisfied within a week of marriage; about 20 per cent find a budget successful; the average adult in this generation was about 10 years old before he knew that babies developed in their mothers' bodies.

There appeared to be a substantial disagreement between educated public opinion and the existing evidence on the following points: A majority of students were not aware that the existing evidence showed that women who had no sex education worthy of the name were as apt to achieve happiness as those who reported some kind of sex instruction (55 per cent expected the opposite); that 75 per cent of married persons said that they would probably remarry if they were now single (the median graduate student estimated only 25 per cent); that the first five years of married life were the happiest, and that the percentage of happiness decreased in the group that had been married more than five years (only 22 per cent of students guessed that this would be so); that the few cases in which the wife was from one to three years older than the husband were more apt to turn out well than the cases following the traditional pattern of older husband (even after hearing the evidence, 90 per cent remained convinced of the contrary); that the marriages of the college graduates in Hamilton's group did not work out as happily as the marriage of the noncollege persons (only 8 per cent of the graduate students of education expected this); that happiness in marriage would be likely to go with a feeling that one's sex desire was below average (only 3 per cent guessed this); that 30 per cent of those having had extramarital sex intercourse were nevertheless happy in their marriages (the students estimated about 19 per cent); that 74 per cent of the men and 70 per cent of the women in Hamilton's unusually successful group confessed themselves lacking in self-confidence to a serious

degree (the students estimated 24 per cent); that 83 per cent of the men and 58 per cent of the women continued some masturbation after marriage (the students estimated only 15 per cent of men and 14 per cent of women); that marriages with children were no happier than those without (82 per cent of the students believed that marriages with children were the happier); that objections to children came more frequently from men than from women, only 34 per cent anticipating the much larger number of cases in which Hamilton found the men raising objections (the majority of students believed the very opposite); that the age range for the establishment of catamenia was from 10 to 19½ years (and not within the narrow limits of 12 to 15 as was generally thought); that as many women as men found their spouse sexually attractive. The tendency among the students was to express the belief that it was the male who valued the sexual attractiveness in the spouse, and that sexual adequacy in the male is more essential to mental happiness. More than half (54 per cent) were of the opinion that sex adequacy in the female is of dominant importance to marital success.

Only the bare outlines of the statistical work can be given, and the reader is referred to the original article for specific figures and more detailed analyses. From a perusal of their findings, the authors conclude that the table on scientific studies of sexual questions has engendered a veritable babel of extreme and contradictory concepts, and a general observation made from this study concerns the fact that no one type of person was outstandingly well informed. Men were no better informed than women, married persons had no larger proportion of correct estimates than single persons, and whatever advantages accrued to age on some points were balanced by an equivalent advantage to youth at other points. Selection of a wise counselor on matters of sex will have to be a matter of personal qualifications and may well be independent of age, sex or marital status.

Wise, Howard, R. I.

ANALYSIS AND STRUCTURE OF A TRANSIENT HYPOMANIA. BERTRAM D. LEWIN, *Psychoanalyt. Quart.* 1:43, 1932.

In this paper the author presents first a portion of the case of a woman, aged 30, with predominantly hysterical symptoms, the initial symptoms being marked photophobia and sensitiveness to noises. One month after analysis began a definite hypomanic attack of seven days' duration developed. This attack was precipitated by a definite incident. Arriving a quarter of an hour earlier than usual, she heard the analyst conversing with a woman. That hour she lay morosely on the couch, refusing to speak, and she rushed to the bathroom at the end of the hour and vigorously washed her hands. On the next day she told the analyst that she had fantasied that he was having sexual relations with the woman, and that she had been sexually excited and angry. Her associations then dealt with persons being surprised in the act of coitus, attempts she had made to spy on her former lover and the mistress who succeeded her and stories of analysts seducing patients.

From the content of the hypomania it was apparent that the patient reacted to her eavesdropping on the analyst and the woman as if she had overheard sexual relations; that her reaction was a transient hypomania in which she was acting out a coitus from the standpoint of both sexes, culminating in a fantasy of taking both rôles in the sex act at practically the same time. It is interesting that in the analysis, the eye and ear symptoms returned after the transient hypomania while she was working through her identification with the observing brother, just as they arose after she was removed from the parents' room. Actually she had slept in the parents' room until the birth of her brother. Now she was removed to the room adjoining. The brother occupied her place near the parents; along with the more usual penis envy and oral envy, her big grudge against the brother was visual and auditory, that is, he was able to hear and see more than she. In the next room, where she slept from 6 till 14, the symptoms really began. As early as 8, her vision was disturbed, so that notes blurred when she tried to play music. She could not sleep if there was the slightest ray of light in the room. Her auditory acuity dates back to this period, as does her theory of

sexual relations in the standing or kneeling position, with the participants completely immobile.

This case raises some interesting theoretical points: 1. She had an incomplete superego; she included a large amount of oral libido in the vaginal cathexis, and for her coitus meant not only a relation with an object but also a vaginal incorporation of the partner, who transitorily becomes a "superego." In her introspective account of coitus, the patient described this rôle of the sexual partner well. Interestingly enough, she went further and openly identified attempts at mystical union with God, the church, or woman's suffrage with the sexual act, and these ideals with her sexual object. That she identified her lover not only with her superego but also with her mother's breast is clear from her fantasy during fellatio—that his penis was a mother's nipple and she a babe. There is consequently an equation of several terms: fusion with superego = fusion with ideals (God) in religious transport = fusion with man in coitus = fusion with mother's breast. That her religious experiences, her love affair and the transient episode during the analysis were structurally fusions of ego and superego and "clinically" hypomanic states merely corroborates Freud's assertion that mania is a fusion of the ego with its superego. She spoke in the hypomanic episode, now as if she were the incorporating party, now as if the incorporated. From this one sees that the hypomanic ego included both elements of the combination, so that she could speak either as if she were the original ego or the superego. The new ego was ego plus superego.

2. The author then asks the question: If a hypomanic state is structurally the same as an identification with both parties in coitus, is it possible to derive the formal, general and characteristic elements of the neurosis from the elements present in the coitus observation? It is known that specific elements in a neurosis corresponded to specific or accidental elements in an observation of coitus. But can the grosser, more general features which are differentially diagnostic in psychiatric nosology be thus derived? As an answer Lewin presents analogous elements:

<i>Coitus Observation</i>	<i>Hypomanic Attack</i>
Two active participants	Bisexual productions
Motion of adults. Immobility of child	Motor overactivity
Sounds from adults	Talkativeness, noisiness
Sexual excitement	Sexual excitement
Adults' orgasm. Child's orgasmic equivalent	"Expulsions" (Abraham)
A "celebration"	A celebration (Freud)
Stimulation of fantasy in child	Flight of ideas
"Violence" of adults	Aggressive symptoms (?)

3. The next problem is the nature of the new "hypomanic" ego resulting from the fusion of the ego and superego. It contains sexualized identifications with the father and mother. There has been a reversal of the process which leads to superego formation. The superego has disappeared and the relationship with the first libidinal objects for the id, the parents, represented in the ego by identifications, was resexualized. The nature of the new ego may best be ascertained by considering the typical mode of defense used by the patient, namely, denial. She denied or repudiated painful critique from the environment or from the reality testing apparatus, and altered to this extent her contact with the real world. The "hypomanic" ego then was essentially a purified pleasure-ego, introjecting the sources of pleasure and rejecting the sources of pain.

The author summarizes the personality structure as seen in this transient hypomanic attack. The ego fused with the superego by an oral mechanism. The resultant "hypomanic ego" was a purified pleasure-ego, ingesting the sources of pleasure, ejecting the sources of pain by denying. The new ego contained the parental identifications previously in the superego. These identifications were sexualized, and the sadism previously emanating from the superego, but now in the ego, was turned against the environment, partly in sublimations, partly in denial of parts of reality or the intrapsychic representatives of reality which might cause pain. The content of the hypomanic attack was an identification with both parents in coitus

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ARTERIAL ENCEPHALOGRAPHY AND ITS VALUE IN THE DIAGNOSIS OF BRAIN TUMORS. EGAS MONIZ, AMANDIO PINTO and ALMEIDA LIMA, Surg., Gynec. & Obst. **53**:155 (Aug.) 1931.

The study of arterial encephalography dates back to 1927, when Moniz read a paper on the subject before the Society for Neurology and Academy of Medicine, Paris (Moniz, Egas: L'encéphalographie artérielle, son importance dans la localisation des tumeurs cérébrales, *Rev. neurol.* **2**:72 [July] 1927). Since then, Moniz and his co-workers claim uniform success in localizing tumors of the brain by the method, which consists, briefly, of injection into the internal carotids of an opaque liquid (from 22 to 25 per cent chemically pure, freshly prepared, watery solution of sodium iodide), thus rendering impervious to the x-rays the whole system of the arteries of the brain. The alterations in the arterial system produced by tumors are a means of localizing the latter. The arteriographic study is easily made and may be used in most cases of tumor of the brain, but it should not be used in the presence of sclerosis of cerebral arteries and should not be repeated in the same case, according to the writers.

The patient is given 30 cg. of phenobarbital both on the night before and early on the day of examination. This is said to help to avoid epileptic attacks, which may follow the injection. As it is impossible to make the injection directly, it is necessary to expose the carotids. At first, injection directly into the internal carotid was attempted, but at times this was found difficult, especially when the bifurcation of the common carotid was located further up than usual. To avoid this difficulty the injection was made directly into the common carotid, temporarily obliterating the external carotid. The first procedure is advised when possible. Local anesthesia was always used, but this need not mean that light general anesthesia cannot be used in patients with precarious mental conditions.

With the patient in the classic position for ligation of the carotid, the artery is exposed through an incision along the anterior border of the sternocleidomastoid muscle. The internal carotid is isolated if possible, but if not the external carotid is isolated in readiness for obliteration at the proper moment, and the injection is made into the common carotid. If the internal carotid is isolated, the injection is made into it.

The patient is placed in the required position under an x-ray bulb; that is, he lies on the side opposite the one into which the injection is to be made, with the head supported in such a way that the frame of the apparatus on which he lies remains in the horizontal position. The apparatus will be horizontal if the line of the patient's eyes is vertical. The head is held in a fixed position, and movement is prevented by means of a bandage. A syringe of 10 cc. capacity, filled with chemically pure, recently prepared, watery (from 22 to 25 per cent) solution of iodide of sodium is in readiness, to which is attached a platinum needle 8 cm. by 1 mm., made in the form of a bayonet. As soon as the attendant gives the signal that the apparatus is in readiness, the artery is punctured by means of the needle. This does not cause the patient any pain. It has been the custom when making the puncture in the common carotid to introduce the needle far enough within the lumen of the artery to enter the internal carotid. In this way the injection is made just as though it had been started from the internal carotid. When the artery is entered, the modified Martins forceps, which had been placed loosely over the external carotid and below the needle in the common carotid (only one clamp below the needle in the internal carotid if the needle is inserted in that vessel), are closed down. It is essential that the injection then be made quickly, and that the radiogram be made at the very moment at which the quantity of fluid injected seems to be sufficient. Excellent radiograms have been obtained with 4 or 5 cc., but the authors prefer 6 or 7 cc. for adults (a little less in women) and from 2 to 3 cc. for children.

Once the film is developed and found satisfactory, the operative incision is dealt with in the usual manner. If the photograph does not reveal the arteries sufficiently, the injection is repeated.

The authors have made approximately two hundred encephalograms in one hundred patients with this method, and report that except in the presence of

arteriosclerosis and in instances in which an iodide solution not sufficiently pure was used no difficulties were experienced. No numerical report of mortality or morbidity was made.

Localizing diagnoses from arteriograms were made by considering the following points: (1) location and irregularity of the sylvian group of arteries on one side as compared to the other; (2) location of visible adventitious circulation supplying a tumor; (3) position and visibility of the anterior cerebral vessels of the two sides; (4) abnormalities in filling or position of the median and posterior cerebral arteries and the arteries around the corpus callosum.

By developing cerebral arteriography Moniz and his co-workers have brought forth a means of intracranial localization which may well prove to be of value. To inject 23 per cent sodium iodide solution directly into the cerebral vessels seems radical, and the occasional convulsions that are mentioned indicate that the procedure is not without some danger. However, encephalography by the injection of air, which is now so widely used with good results, was not without its disasters at the beginning of its development, and further application of arterial encephalography may justify its universal acceptance.

GAGE, Montreal, Canada.

VITAMIN DEFICIENCIES AND NERVOUS SYSTEM LESIONS. J. A. M. A. **99**:137 (July 9) 1932.

Since Eijkman (Eine beriberiähnliche Krankheit der Hühner, *Virchows Arch. f. path. Anat.* **148**:523, 1897) showed that noninflammatory atrophic degeneration of the medullary sheaths of peripheral nerves occurred in hens fed on a diet of polished rice, it has been known that dietary deficiencies cause lesions of the nervous system. The factor responsible for this particular morphologic change was shown by Woollard (The Nature of the Structural Changes in Nerve Endings in Starvation and in Beriberi, *J. Anat.* **61**:283 [April] 1927) and others to be produced by a deficiency of vitamin B. Recently it has been found that what has heretofore been called vitamin B is really a mixture of at least two components; namely, the heat-labile antineuritic factor and a thermostabile substance, the absence of which is thought to produce pellagra. Stern and Findlay (The Nervous System in Rats Fed on Diets Deficient in Vitamins B<sub>1</sub> and B<sub>2</sub>, *J. Path. & Bact.* **32**:63 [Jan.] 1929) studied the changes in the nervous system of rats fed diets deficient in vitamin B (antineuritic component) and vitamin G (pellagra-preventive factor), respectively. In the first group of animals, they found chromatolytic changes in the ganglion cells of the spinal cord and early degeneration of the myelin of the peripheral nerves. In the second group, the changes consisted of swelling and vacuolization of the anterior horn cells of the spinal cord with the deposition in them of lipochrome pigment. Recently Zimmerman and Burack (Lesions of the Nervous System Resulting from Deficiency of the Vitamin B Complex, *Arch. Path.* **13**:207 [Feb.] 1932) have reported extensive demyelination of the peripheral nerves of dogs on a diet deficient in vitamin B, but they found similar though less marked changes in dogs that were entirely deprived of food except for adequate vitamin B complex in the form of vitavose. In animals that were partially or wholly on a diet deficient in vitamin G there were present degenerative lesions in the vermis cerebelli, the restiform bodies and the fasciculus gracilis of the spinal cord, as well as demyelination of the peripheral nerves. Degeneration of the myelin sheaths of the median dorsal columns was found by Winkelmann (Beiträge zur Neurohistopathologie der Pellagra, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **102**:38, 1926) in a case of human pellagra, and both Pentschew (Ueber die Histopathologie des Zentralnervensystems bei der Psychosis pellagrosa, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **118**:17, 1928) and Langworthy (Lesions of the Central Nervous System Characteristic of Pellagra, *Brain* **54**:291 [Sept.] 1931) reported disseminated foci of demyelination in the spinal cord in similar cases.

It has been held that deficiencies in the vitamin B complex alone were responsible for lesions of the nervous system, but in 1931 Pappenheimer and Goettsch (A Cerebellar Disorder in Chicks, Apparently of Nutritional Origin, *J. Exper. Med.* **53**:11 [Jan.] 1931) described softenings in the cerebellum in chicks which

they attributed to a lack of vitamin E. These lesions were in every way identical with those described by Zimmerman and Burack in their dogs subsisting on a diet deficient in vitamin G. Mellanby (*The Experimental Production and Prevention of Degeneration in the Spinal Cord*, *Brain* **54**:247 [Sept.] 1931), too, has reported observations on puppies deprived of vitamin A which developed degenerative changes in the form of demyelination of the nerve fibers of the spinal cord similar to the lesions seen in subacute combined degeneration. Furthermore, Hess (*Focal Degeneration of the Lumbar Cord in a Case of Infantile Scurvy*, *J. Infect. Dis.* **23**:438 [Nov.] 1918) described focal degeneration of the lumbar cord in a case of infantile scurvy complicated by rickets.

If it can be assumed that, in the experimental work, lesions in the nervous system are produced as the result of single rather than multiple vitamin deficiencies, it must be granted that a large variety of vitamins play a specific part in the production of these lesions. Or, at least, any one of them can play an important contributory part to some factor, as yet entirely unknown, which is activated by them and alone produces the lesions. Which of these factors is responsible for the changes observed must await solution by the experimental method. It is more than likely that little in the way of positive proof can be adduced from the human cases of deficiency diseases associated with changes in the nervous system, as they almost certainly represent multiple deficiencies.

EDITORIAL.

LESIONS OF THE NERVOUS SYSTEM RESULTING FROM DEFICIENCY OF THE VITAMIN B COMPLEX. H. M. ZIMMERMAN and ETHEL BURACK, Arch. Path. **13**:207 (Feb.) 1932.

It has long been known that deficiency of vitamin B leads to well defined neuromuscular symptoms. In animals these symptoms are manifested as spastic paralysis, ataxia, opisthotonos and convulsions. In 1897, Eijkman described non-inflammatory atrophic degeneration of the medullary sheaths of the nerves in hens fed on a diet of polished rice. He also noted chromatolysis and atrophy of the ganglion cells of the anterior horns of the spinal cord. Vedder and Clark, in 1912, made similar observations in rice-fed fowls. They found, in addition, chromatolysis in the dorsal and ventral root ganglions and degeneration in the nerve roots and spinal cord involving the myelin sheaths and axis cylinders. Pigeons fed on autoclaved rice were found by McCarrison to have degenerated fibers throughout the spinal cord and in the nerve roots. Furthermore, the sciatic nerves in his animals showed degenerated fibers in 88 per cent of cases, and the vagus nerves in about 63 per cent. He concluded that the paralytic symptoms were due mainly to impaired functional activity of nerve cells and, much more rarely, to their degeneration.

In none of the twelve animals studied in this contribution was there any gross evidence of disease in the central and peripheral nervous systems. Microscopically, a peripheral polyneuritis, in the sense of myelin degeneration, was found in the sciatic, median and ulnar nerves, the brachial plexuses and the vagus nerves, decreasing in severity in the order named and involving all the animals except the two normal controls. The neuritis implicated the bilateral nerves to an equal degree, was as marked in the proximal as in the distal portions of each nerve and appeared to parallel in severity the duration of the clinical symptoms, except in the starvation controls, in which paralytic manifestations did not develop.

In none of the animals were changes found in the spinal nerve roots. Tigrolysis, pigmentation and acute swelling were present in an occasional anterior horn motor cell in the spinal cords of all the animals. An occasional black ringlet of myelin degeneration was found by the Marchi method in the experimental animals, as well as in the controls. Sudan III preparations of the spinal cord were invariably normal, as were the modified Weigert preparations, except in dog 1. In this animal (which was on a highly purified diet during the whole course of the experiment) there was degeneration of the fasciculus gracilis demonstrable not only in Kulschitsky preparations, but in Marchi and Nissl preparations as well. With the latter stains, it was seen that the median dorsal fasciculi contained regressive glia—microglia and myeloclasts.

In Spielmeyer preparations of all the spinal cords of the normal controls, the fasting controls and the animals on vitamin B-deficient diet, there were found disseminated, large, irregular, unstained areas involving motor as well as sensory tracts. In serial sections stained by this method it was noted that the unstained patches in no two consecutive preparations occurred in precisely the same location.

In his conclusions the author states that extensive demyelination was present in the sciatic, median, ulnar and vagus nerves and in the brachial plexuses of dogs deprived of the water-soluble B vitamins. The destruction of myelin was most severe in the sciatic and least severe in the vagus nerves of all the animals subsisting on a vitamin B deficient ration. The extent of the anatomic alterations in the peripheral nerves varied in direct proportion to the severity and duration of the paralytic symptoms. Peripheral polyneuritis of the same type, but of less degree, was present in the control animals, which were entirely deprived of food but supplied with an adequate amount of the B complex. Changes in the ganglion cells and disseminated foci of myelin destruction in the brain or spinal cord could not be held responsible for the clinical symptoms of this nutritional disorder. Dogs deprived wholly or in part of the thermostable B factor showed large zones of degeneration and vascular proliferation in the vermis of the cerebellum and in the region of the substantia gelatinosa rolandi. The dog that had subsisted throughout the entire experimental period on the highly purified ration deficient only in the heat-stable factor (B) evidenced degeneration in the fasciculus gracilis of the spinal cord.

WINKELMAN, Philadelphia.

THE CATARACT OF POSTOPERATIVE TETANY. C. S. O'BRIEN, Arch. Ophth. 7: 71 (Jan.) 1932.

The association of cataract with tetany has been known for many years. In postoperative tetany one must consider interference with the function of the parathyroid glands. They apparently control calcium metabolism. Postoperative tetany or tetania strumipriva appears, as a rule, within from forty-eight to seventy-two hours after thyroidectomy. The usual onset is with tingling and tonic spasms in both hands and arms. During the spasm the hands may assume a peculiar attitude known as the obstetrician's hands. In severe cases cramps may be present also in the feet and legs, or they may even become generalized (epileptiform), and there may possibly be dyspnea, choking, difficulty in speech or cardiac involvement. In the severe forms death may ensue. The serum calcium of the blood is greatly reduced, and the phosphorus is increased. Usually the condition is recognized, and the administration of calcium and the hormone of the parathyroid glands control most of the symptoms.

In mild forms of tetany, even though untreated, the symptoms may improve, and only a condition of latent tetany may remain. The diagnosis of latent postoperative tetany depends on the demonstration of hyperexcitability of the peripheral nervous system, certain trophic changes in the epithelial structures and low blood serum calcium combined with a high serum phosphorus. Erb's sign, hyperirritability of the nerves on application of the galvanic current, may be elicited. Chvostek's sign may be present; i. e., light tapping of the facial nerve over the area of the parotid gland produces twitchings of the muscles of the face. Trousseau's sign is sometimes present, i. e., muscular contractions of the forearm and hand on constriction of the arm. Trophic disturbances are frequently present; cataracts may develop, and other epithelial structures may be affected; e. g., the hair may fall out, the nails may be lost, cavities may develop in the teeth, and eczema or pigmentation of the skin may appear. The blood calcium is reduced, and the phosphorus is increased. In a state of latent tetany there are usually no spasms. The history of an operation for goiter, followed for a time by transient and perhaps recurrent cramps, and the discovery of some or all of the findings mentioned may be the only indications of the cause of rapidly developing opacities of the lenses. This condition is not rare from the standpoint of the ophthalmologist.

The author's summary, in part, follows: Rapidly developing bilateral cataracts in presenile persons, especially those of the female sex, may be due to post-operative tetany. In patients of this age one should always think of such a possibility. The diagnosis is made from (1) a history of thyroidectomy followed by spasms of the upper extremities and perhaps of other parts of the body, (2) a low serum calcium of the blood associated with high phosphorus and (3) signs of hyperexcitability of the peripheral nervous system (Erb's, Chvostek's and Trousseau's signs).

Cataracts develop with either manifest or latent tetany, and they advance despite treatment that may control all other manifestations.

Probably there is no pathognomonic picture of this type of cataracta complicata, but it seems that the first changes appear as aggregations of fine opaque granules directly under the anterior and posterior capsules of the lens.

The prognosis should be guarded because of the fact that delayed spontaneous hemorrhages may occur after extraction of the lens. Before and after extraction of such cataracts the patient should receive parathyroid hormone and viosterol, and his calcium intake should be high, in order that the blood and tissues may be in as nearly normal a state as possible.

SPAETH, Philadelphia.

PSYCHOLOGY AND PSYCHIATRY. BERNARD HART, *Ment. Hyg.* **16**:177 (April) 1932.

Each science passes through three stages: (1) a period of collection and enumeration of data, (2) a period of description and classification and (3) a stage of interpretation and application. Psychology now finds itself in the second phase. In its endeavor to assist medicine by supplying the physiologic processes of mental disease, psychology appears to have failed. This is a failure, however, not of psychologic methodology, but rather of scientific stubbornness. The effort was made to select from each psychosis its prominent symptom, such as a delusion or hallucination, and to build around that a disease entity. The inadequacy of such a technic cannot be ascribed to psychology, but must be attributed rather to the orthodoxy of psychiatrists who could see no other method except that used in clinical medicine.

The work of Pavlov and Watson is not, in the sense that Hart uses the term, a contribution to psychology. Their refusal to concern themselves with subjective phenomena, especially consciousness, serves to place them beyond the confines of psychologic workers. Lewis Bruce's demand that psychology and psychiatry be divorced is similarly condemned by the author, who brands it as an "attempt to play Hamlet without the Prince of Denmark." These "organic" or "physiologic" approaches are contrasted by Hart (who hastens to assure his readers that this contrast will not lead him into the "either-or" fallacy) with the psychic or "functional" aspect of the problem. The latter method, he agrees, is imperfect, but this should stimulate psychologists to improve rather than to discard their weapons. In any event, psychic concepts should not be rejected if they fail to explain certain phenomena, but only if they contradict them.

Hart reviews briefly the history of psychologic psychiatry, commenting sadly on the failure of the promising attack made by Kraepelin which was to terminate in "an orgy of pigeon-holing." Charcot's proposal that the fundamental phenomena of hysteria might be ideas was a landmark in this history, subsequently developed by Janet and Freud. It was Janet who first used "pure psychology" as an explanation for the neurosis. His willingness to attach this "functional" explanation to such apparently organic signs as anesthesia or paralysis was a significant forward step. It was not until the time of Freud, however, that any one thought of assigning a purpose or a meaning to phenomena in purely psychic terms. His refusal to accept the traditional limitations of psychology was an epoch-making event, for he demonstrated that the manifestations, whether organic or purely subjective, of neuroses and psychoses could be explained adequately and reasonably on purely psychic grounds. In view of the adequacy of this method, Hart sees no reason why the psychologist should court so assiduously

the physiologic approach. Mechanism, he insists, is not synonymous with science; indeed the physicist himself is inclining more to abstract ideas and is slowly abandoning mechanism. He quotes Jeanes: "Knowledge is heading towards a non-mechanical universe, which begins to look a little more like thought and a little less like a machine. Mind, no longer an accidental intruder, is perhaps a creator or governor of matter." With increasing success nature is being interpreted in terms of pure mathematics; yet this is not scientific in the sense that mathematicians formulate their concepts out of their inner consciousness without drawing to any appreciable extent on their experience in the outer world. The psychologist, therefore, should hesitate before accepting the scientific road as the only one which leads to truth.

DAVIDSON, Newark, N. J.

RELATIONSHIP OF ORAL AND PHARYNGEAL ABNORMALITIES TO SPEECH. DON CHALMERS LYONS, Arch. Otolaryng. 15:734 (May) 1932.

The production of vocal sounds or phonation depends on the perfect working of all parts of the speaking machine. Speech is produced by passage of expired air through an elastic tube. Quality, timbre or type depends on the ability of the tongue and velum to stop the air. The mechanism is complex; nerve centers in the cerebrum and other parts of the brain participate. Abnormality is any conspicuous defect from the usual speech pattern and may be due to changes in the nervous system or air passages. Speech defects have been classified as follows: (1) dysarthria, inarticulateness, labored speech and ataxic speech; (2) dyslalia, lisping, mutism, delayed speech and uraniscologia or cleft plate speech; (3) dyslogia, or difficulties in expression of ideas by speech, incoherent speech and those defects due to different psychoses; (4) dysphasia, due to a weakness in the mental imagery, as in grouping speech; (5) dyshemia, due to psychoneuroses or fright or passion, for example, stuttering or stammering; (6) defects of the voice itself, as aphonia or voicelessness, baryphonia or thick voice, hypophonia or whispering and rhinophonia or nasal voice; (7) dysrhythmia, or the defects of rhythm, as in breathing defects. Many of these defects can be remedied only by training in speech; others, by repairing the mechanism surgically or medically. Cleft palate is the most common defect. Its correction should start soon after birth. One should wait until the patient is 2 years of age before the soft palate is repaired. Special training in addition to surgical measures is required. Tumors of the tongue, abnormally long or thickened uvula, bifid or double uvula, improper development of the palate, enlarged tonsils and adenoids, nasal polypi, deviation of the nasal septum, hypertrophied turbinates, stenosis of the larynx, chronic laryngitis, sinus disease, postdiphtheritic paralysis, perichondritis of the laryngeal and nasal cartilages and defective hearing require surgical or medical attention. The tongue may be completely removed without losing all the power of speech. Intranasal obstructions interfere with the resonance necessary for the correct sounding of *m* and *n*. Defective hearing and abnormalities of the lips impair speech. There are many possible dental causes, such as a thick sheet of vulcanite over the palate, the bite of the teeth and the escape of air, which cause lisping. Some people make no effort to acquire new habits of mastication following the loss of their teeth; this is also true of speech. Defects of speech are stuttering, stammering, falsetto speech and lisping. They have been attributed to fear, cerebral congestion, lagging respiration, defective auditory or visual memory and anatomic malformations of the organs of speech. While it may be true that these defects are deep-seated or psychoneurotic, many follow surgical procedures on the palate and teeth or focal infections with changes in the passageway. The subject of defects in speech covers so many ramifications that it was impossible in this paper to do more than touch lightly on some of the phases. The physician and the oral surgeon can put the apparatus in condition so that the teacher has a better chance. More attention should be given to defects of speech as patients with defects of speech often suffer also from personality deficiencies, social handicaps and mental and physical disorders directly attributable to the abnormal speech.

HUNTER, Philadelphia.

SIGMUND FREUD IN HIS HISTORICAL SETTING. C. G. JUNG, Translated by Cary Baynes, *Character & Personality* 1:48 (Sept.) 1932.

Freud would have one believe that his theory has sprung fully formed from his brain, devoid of any historical roots. Yet clearly this is not the case. Freud grew in the matrix of the decaying morality of the late nineteenth century, when the world was striving frantically to keep alive the religious ethics of the middle ages. By the quality of this environment Freud's contributions have been shaped. The Viennese marked no new ways and heralded no new truths; he destroyed rather the unwholesome smugness of the morality of his day. For example, in revolt against the nauseating sentiment of the pure babe and the sanctified mother, he ascribed to the suckling a sexual urge. He implied that the apotheosis of motherhood as holy must be an attempt to conceal something very unholy; unhappily, however, he blackened the babe rather than the mother. In strict truth, it must be admitted that to describe the babe's urge for its mother's breast as sexual attraction is merely to assign a new word to an old idea; the interpretation is probably incorrect, and in any case its accuracy is of little importance. What is important in this example, however, is that Freud dared to attack the altogether horrible idea of maternal sanctity and infantile pureness.

Characteristic of Freud is the fact that he looks backward, never forward; that he destroys old ideas but constructs no valid new ones. After all, what can be done about an incest wish or any other subconscious incompatibility? It is possible to make out a case for repression as the best thing to do with these wishes. That these urges are, as the psychoanalysts say, "sublimated" is a pious fiction, an outlet for inopportune questions. One of the serious charges against the disciples of Freud is that their interest is always in where things come from, never in where they are going. A second charge against them is their definite, although unconfessed, belief that naturally there must be something scandalous in every incomprehensible situation. If the poorly understood chapters in the lives of great men could not be explained on the basis of Oedipus complexes or castration urges, Freud's task of exposing the darkness behind the false façade of the world would not be fulfilled. Indeed, Freud is, as it were, under compulsion to uncover the sediment of the human soul and to demonstrate that it is most shocking.

The freudian hypothesis is a partial truth, with the fanaticism of an inquisition and the rigidity of a dogma; it is, therefore, in no sense a science. It is curiously localized in time to the early twentieth century, in place to Caucasian civilization. It assumes most incorrectly that a neurosis is a disease found only in Europe and only in the first quarter of the twentieth century. Psychoanalysts receive no instructions above the management of neurotic persons who are not in need of sexual enlightenment or improved sexual adjustment. The entire freudian philosophy is built around the inadequacy of sexual repression, which is after all a minor matter in the field of universal science. At other times and in other places, sexual repression is neither as potent nor as significant as in Victorian Europe. How can Freud claim to have sired a science, when this "science" is so limited in scope and applicability? Freud has not penetrated into that deeper layer of what is common to all humanity; to do so would be infidelity to his cultural-historical task. But he *has* accomplished a task; for this the world owes him gratitude. It is properly a great man's life work.

DAVIDSON, Newark, N. J.

SOCIAL IMPLICATIONS OF PSYCHIATRY. A. E. DAVIES, *Brit. J. M. Psychol.* 12:15 (July) 1932.

The writer believes that, while the study of the psychology of behavior is deservedly in the foreground in the field of psychiatry today, too little emphasis is placed on the study of social and moral factors, and that psychiatry has its part to play in the enthronement of morality in the modern world. The present interest in psychiatry is described as originating in humanitarian sentiment, this later being stimulated by a public conscience feeling its responsibility for the mentally sick dependent on public charity.

An interesting description is given of present schools of psychiatry, which are classified as those of neurologic psychiatry and of psychologic psychiatry. The neurologic psychiatrist is described as holding the view that nervous and mental disease is the product of lesions of the nerves alone. The psychologic psychiatrist believes that psychogenic factors can cause mental disease. The question is raised, how can the neurologic psychiatrist, holding the view that psychogenic factors never cause mental disorder, consistently treat the patients in cases in which no organic basis can be found if he refuses to admit the possibility of any other than organic factors as complicating the situation?

The psychologic psychiatrists fall into two groups, analytic and nonanalytic. It is held that in analytic (or psychoanalytic) thinking too much stress is laid on the sex problem, and that there is too little awareness of social and moral factors. Davies give a detailed discussion of the differences between the Freudian and the Zurich schools of psychoanalysis. He states that, according to the thinking of these schools, man is richly endowed with a social sense, and advances the criticism that even if "social imperatives" (Jung) are instinctive tendencies, no distinction is drawn between action at the level of the instincts and reasoned behavior. For example, psychoanalysts lay too little emphasis on public opinion and what it may mean in the life of the individual.

Both analysts and nonanalysts should record more carefully the social factors that emerge in the study of cases, connect them with the symptoms and describe how the patient deals with these problems. The psychiatrist's main business is with the exciting cause of mental disease, and it is chiefly for the light they throw on this that he inquires into predisposing causes. The writer offers a tentative plan for grouping the factors that determine the behavior of a person at a given time in his life history. Such categories as sociopersonal, economicopersonal and ethicopersonal, and sociosexual, ethicosexual and maritosexual are mentioned, meaning that the patient's behavior when under consideration was aimed at maintaining an adjustment in these fields. In a case that is described, the knowledge of the factors motivating the patient's behavior, as set forth by the classification, is utilized by the psychiatrist in interpreting to the patient what the exciting factor in his illness is and why he reacts as he does in this particular situation.

ALLEN, Philadelphia.

ATYPICAL MIGRAINE. O. U. GEYMANOVITCH, Ukrain. Psychoneurol. Inst. **20**:7, 1932.

Neuropathologists are familiar with the established type of migraine, the status hemicanicus of Moebius. Paulian described a case of ophthalmoplegic migraine with involvement of the hypophysis. Migraine becomes a syndrome of a mechanical order. A mechanovegetative hypothesis can be formulated: Migraine is a syndrome of the loss of function of the midbrain with a mechanical genesis; compression, for example. Occasionally, an attack of migraine may be caused by disease of the upper sympathetic ganglion. Oppenheim observed a case of hemicrania of the left side with narrowing of the orbital aperture in a woman who never perspired. These are instances of the neurocompression type. Great difficulties arise in the semeiologic elucidation of cases of diffuse headache, and in the differentiation of cephalic symptoms with signs of meningeal irritation. The neuralgic pains of the trigeminus possibly have their origin in meningeal irritation (Wernicke, Lewandowsky). The analysis of accessory neuromyelic elements occasions considerable difficulties. The atypical forms of migraine derive their importance from the fact that they enlarge the concept of the semeiology of migraine, besides shedding light on its mechanism. In a brief consideration of such atypical forms, the author mentions a group of cases with ocular symptoms associated with disturbance of the cranial nerves and its variants. In one case he observed optic alexia, which alternated with sensory aphasia. Paresthesias were observed most frequently on the same side as hemicrania, but occasionally they

were heterolateral and even bilateral. He had also seen a patient with sensory disturbances of the spinal segmentary type. In circulatory disturbances of a central type one may observe, with the commoner horizontal type of sensory disturbances, a rarer vertical type. Cardiac states are frequently associated with migraine, giving rise to sensory disturbances usually, though not necessarily, on the left side. Sensory jacksonian forms likewise occur. The so-called vagal attacks of Gowers may progress into an epileptic form. This symptom-complex is most complicated, and may be traced to an organic genesis. The greatest difference of opinion exists regarding the ocular palsies. Richter postulates that an attack of migraine is a special form of a vascular crisis conditioned by the spasm of the vertebral or the basilar artery or both posterior cerebral arteries. This vascular area is under the control of the upper sympathetic innervation. The association of myelalgia with migraine is possibly of sympathetic origin, being produced by the same circulatory disturbance as the migraine itself. Persons who have migraine are frequently arthritic. The author has not observed the phenomenon of white dermographia in patients with vestibular symptoms.

EDITOR'S ABSTRACT.

**PATHOGENIC RELATIONSHIPS BETWEEN TRAUMATISMS AND CERTAIN ORGANIC DISEASES OF THE CENTRAL NERVOUS SYSTEM. GIUNIO CATOLA, Encénhale 27:292 (April) 1932.**

The author has lately observed several cases of organic disease of the nervous system in which the origin might be considered obscure unless one gave credence to the effects of certain unique and strong traumatisms. The first case was one of cerebral tumor. There has always been discussion as to the possible place of trauma in such neoplasms, and the pro and con arguments are summarized here. A man, aged 59, suffered a severe blow in the right parietal region, with symptoms of cerebral concussion. Two months later, all evidence of the injury was gone, but about this time jacksonian convulsions of the left side commenced. As these increased, together with advancing paralysis of the left side, a diagnosis of neoplasm of the right rolandic area was made. Surgical intervention was advised, but when the dura was opened no tumor appeared. However, a mass was found deep in the centrum ovale. This was, of course, not removable, and after some temporary relief due to relief of pressure the patient gradually became worse. The lesion was directly beneath the traumatized zone, and the case for a causal relationship looked unusually strong. Fortunately, the author learned that for some time preceding the trauma the patient had experienced attacks of severe vertigo. The conclusion is that the trauma was secondary to an already existing neoplasm.

The second case was that of a man previously in excellent health, in whom parkinsonism rapidly developed two months after a blow on the head. The author believes that the evidence of an association of cause and result is very probable.

The third case is that of another parkinsonian patient, a woman, aged 57, in whom the syndrome developed fifteen days after a blow on the head. The symptoms appeared first on the corresponding side, but later became bilateral and thus made more doubtful the relationship. It is suggested that vascular predisposition existed, and that the rarity of such syndromes following trauma of the head in the war is due to the youth of the soldiers and the comparative absence of such vascular predisposition.

The last case was one of syringomyelia, in which the relationship is not clear, but in which it is suggested that syringomyelia might develop more easily on an old scar tissue-producing trauma.

The conclusion is that even the most apparently clearcut instances of traumatic etiology of organic disease of the nervous system are likely to be invalidated by knowledge of all the factors.

ANDERSON, Los Angeles.

SYNESTHESIA IN PSYCHICALLY ABNORMAL PERSONS. G. KLOOS, Arch. f. Psychiat. **94**:417 (June) 1931.

Kloos reports a series of studies in a psychopathic personality of shiftless, pseudologic type, with mood swings, in which one of the outstanding symptoms was the occurrence of synesthetic experiences. The study is concerned not so much with the description of these experiences as with the attempt to determine their mechanisms. Fundamentally, there seems to be a definite relationship between the synesthesia and the experience on which it is built up. This relationship can be seen to exist in respect to the intensity, rhythm and emotional tone of the experience itself and of the synesthesia. From this point of view one can regard the synesthetic phenomenon as a form of expression indicative of the underlying occurrences within the person when he is subjected to the particular experience in question. The synesthesias, therefore, may be looked on as special forms wherein something observable by any sense organ (such as a color and sound) gains in complexity and richness of experience by the accompanying functions of other sense organs.

The occurrence of this phenomenon is furthermore intimately related to the peculiarities in the personality of the subject. These personalities usually show such characteristics as increased sensory impressionability, increased power of imagination, a more complex form of imagery or a retarded development or a temporary decrease of the rational critical functions. In schizoid or schizophrenic persons, particularly those of the romantic and dreamy type, one finds these phenomena frequently. Then, again, an affinity with these phenomena is found in hysterical persons, in psychopathic and in cyclothymic personalities. They are not prone to occur in organic diseases of the brain. When these phenomena occur with a high degree of intensity and tend to control the waking state of the person most of the time, they must be regarded as pathologic. In such persons, synesthesia must be regarded as a sign of retardation of the development of a normal degree of intellectual differentiation.

MALAMUD, Iowa City.

VEGETATIVE ASYMMETRY: PAROTID SYNDROME IN SYRINGOMYELIA. S. D. KAMINSKY, Ukrain. Psychoneurol. Inst. **20**:41, 1932.

Kaminsky describes a syndrome characterized by the appearance of redness in the central portion of the cheek, followed by sweating, especially if the tongue is stimulated by sour or salty substances. This syndrome is most often observed after severe parotitis. These secretory and vasomotor disturbances correspond to the distribution of the trigeminal and the auriculotemporal nerves. Many authors refer to the disturbances as the syndrome of the auriculotemporal nerve, and believe the origin to be reflex. The fact that the syndrome is frequently preceded by parotitis suggests a peripheral lesion of the nerve paths. Many hypotheses have been advanced to explain its mechanism, one of which is the altered blood supply after suppurative lesions of the parotid and after surgical interventions. Brown-Séquard, who had never had parotitis, observed the phenomenon in himself. He believed it to be physiologic, provoked by a pathologic process. The irritation was furnished by the gustatory fibers of the tongue. Higier implicated the vasodilator fibers of the parotid gland the center of which is in the inferior salivary nucleus. The author describes his case in which a patient had syringomyelia without a preceding parotitis. According to Müller, the path which connects gustatory fibers with a branch of the trigeminus proceeds to the pons, from there to the cerebellum and then to the nucleus terminalis, the primary center of taste. Nearby is the plexus of Kohnstamm, giving origin to the secretory fibers of the parotid gland. This path passes as the nervus petrosus superficialis minor to the otic ganglion and from there emerges on the periphery together with the auriculotemporal nerve. Through the same otic ganglion pass the fibers of the superior cervical ganglion, as do other fibers of the vegetative system, such

as those of the vasodilator nerves. The author concludes that the reflex action of vasodilatation and of sweating observed in peripheral lesions (parotitis) may occur in instances of isolated lesions of the central nervous system.

EDITOR'S ABSTRACT.

SYNDROMES OF DYSTONIA: TWO CASES. M. COSTA, An. assist. a psicop., 1931, p. 199.

Costa emphasizes that, in spite of the continued study, both clinical and anatomicopathologic, on the part of the neurologists of all countries, the knowledge of dystonias, from the point of view of their intimate processes and localization, is very rudimentary. Many authors have tried to establish a nosologic entity, employing such terms as "neurosis of torsion," "dysbasia lordotica progressiva," "dystonia lordotica progressiva," and "progressive spasms of torsion." But confusion still reigns in this field of neurology. Certain types of athetosis, Wilson's disease and pseudosclerosis have been considered by various authors as variants of the same morbid state. In their work on dystonias, Austregesilo and Marques conclude: "There are several clinical variations of a pathologic process that is essentially the same, in which the chief lesion is found in the striatum." The dystonias are characterized by changes in muscular tonus, either by hypertonia or by hypotonia. They may attack one segment of the body, more than one segment or the whole body. As a rule, the face and speech are spared, but there are cases in which these are disturbed, as in case 1 of the author. Most commonly attacked are the neck and the proximal extremities of the limbs, likewise the muscles of the back, which provokes an accentuated lordosis and one of the characteristic postures of the syndrome, whereas in athetosis alone the distal extremities and the face are more involved. In most cases hypotonia and hypertonia are associated. But dystonia may be characterized by pure hypertonia, as in the syndrome of Cécile Vogt and Oppenheim, Wilson's disease and pseudosclerosis. The changes in tonus are due to alterations of tension and relaxation. In the state of relaxation the muscle loses the plastic tonus and becomes very flaccid. In muscles seriously involved, hypertrophy (Bourneville, Hall and Sicard) is observed in certain cases. The author describes in detail his cases in a Negro, aged 26, and in a young unmarried man, aged 28.

EDITOR'S ABSTRACT.

SOME EFFECTS OF HETEROPLASTIC TRANSPLANTATION OF THE EAR VESICLE IN AMBLYSTOMA. DOROTHY RICHARDSON, J. Exper. Zool. **63**:413 (Oct. 5) 1932.

Heteroplastic orthotopic transplantation of the ear between *Amblystoma punctatum* and *A. tigrinum* embryos of the same age, before invagination of the otic vesicle, was done to study the effect of the new environment on the grafts and the effect of the grafts on the development of structures in the hosts. The punctatum vesicle transplanted on tigrinum, while smaller than the normal ear of the host, exceeds in size the normal ear of the donor, possibly due to a stretching of the labyrinth epithelium, since it has more room to expand. The tigrinum vesicle transplanted on punctatum becomes larger than the normal ear of the host, but is smaller than that of the donor control, owing probably to the mechanical limitation of its environment. The tigrinum transplant does not induce the formation of a cartilaginous capsule in proportion to its size, possibly due to the lack of a sufficient number of cartilage-forming cells in the host. The punctatum ear on tigrinum becomes enclosed in a capsule which is large in proportion to the size of the labyrinth. The tigrinum chondroblasts may be more numerous or more active. The basi-occipital and quadrate cartilages show no change in amount of cartilage, but some shift in position. The muscles which have their origin on the capsule of the ear are of the same size on the normal and on the operated sides.

Hyperplasia or hypoplasia is produced on the side of the medulla next to the graft, in punctatum and tigrinum, respectively. The response occurs mainly in the area acustica. No change in Mauthner's cell can be detected. Hyperplasia which may have occurred in the cerebellum is not sufficiently great to be evident.

The results show that the growth of the grafted ears themselves is modified, apparently by the difference in the amount of space afforded in each instance, and that there is a response in the cartilaginous capsule and in the area acustica of the medulla, but none in the other cartilages adjoining the capsule or in the muscles attached to it.

WYMAN, Boston.

ANNEBERG DISEASE (1713-1719). E. SCHENK, Arch. f. Psychiat. **94**:730, 1931.

The author reports an interesting critical analysis of an epidemic of hysterical attacks that occurred in the city of Anneberg from 1713 to 1719. It came in the wake of trying conditions which included fear of an epidemic of plague, markedly increased taxes and general financial depression. It began as a phenomenon shown by isolated children, and then spread to a large proportion of the whole population. It showed many variations in form, such as ocular spasms, stiffening of the arms and legs, blindness, aphonia, peculiar postures, tremors, preaching, pseudo-hallucinations of auditory and visual types and reports of seeing fantastic animals, ghosts, etc. The epidemic took on such proportions that the authorities found it necessary to undertake an investigation in order to ascertain the truth of the belief that the whole thing was due to the activities of witchcraft. They appointed a number of physicians to help in the investigations. Among these, Hopner recognized the condition as being dependent on fear and suspicion, and as being related to the difficult conditions that had existed prior to the development of the epidemic. He stated that medicaments such as were in use at the time for organic disease were not useful here, and recommended isolation of the patients affected, so that their beliefs would not be increased or transmitted to others. Some physicians, however, were of the opinion that the condition was due to witchcraft; this led to the imprisonment of a number of persons who were accused of having practiced witchcraft and having caused the epidemic. It is gratifying that the authorities finally agreed with Hopner. The people accused of witchcraft were freed, and the patients showing the symptoms were treated in the fashion that was advised by Hopner. Most of them were sent to work-houses; others were isolated in different places, and after that the condition was easily controlled.

MALAMUD, Iowa City.

THE OCCURRENCE OF CALCIFICATION IN GLIOMAS. C. B. MASSON, Bull. Neurol. Inst., New York **1**:159 (June) 1931.

This study was undertaken with the object of determining the relative frequency of calcification in gliomas of different types. Material used for the study consisted of one hundred and thirty-one cases of gliomas verified by operation or autopsy. It was found that in seventeen cases the roentgenograms showed more or less evidence of deposit of lime salts in the tumor, an occurrence of approximately 13 per cent. Division of the gliomas into various types showed as follows: astrocytomas, twenty-nine, of which six were calcified; spongioblastomas, thirty, of which six were calcified, and medulloblastomas, twenty-five, of which three were calcified. Calcification was also found in one astroblastoma and one oligodendroglioma. There was no evidence of calcification in any of the thirty-one cases of gliomatous cysts, in the three tuberculous and in the eleven unclassified gliomas. The article is well illustrated with excellent plates. The author states that from roentgenographic plates alone it is impossible to differentiate the type of glioma, and the character of calcification is such that it is seldom possible to differentiate with certainty between a calcium deposit in the gliomatous growth and the results of a similar process in an area of degenerated brain, the result of vascular change, or in an old calcified brain abscess. The author believes that the length of time required for the deposit of salts cannot be determined definitely; however, he thinks that the presence of calcification in a rapidly growing glioma, such as a spongioblastoma, is not an evidence of rapid development of such deposits, as such rapidly growing tumors always

contain areas of well differentiated cells, parts that have probably existed for a longer period; these may be the parts in which the lime salts are lodged.

KUBITSCHKE, St. Louis.

THE RÔLE OF THE PSYCHIATRIC DEPARTMENT IN RELATION TO THE PEDIATRIC DEPARTMENT IN A GENERAL HOSPITAL. ERIC KENT CLARKE, Am. J. Psychiat. **11**:559 (Nov.) 1931.

The absence or unsatisfactory position of the psychiatric clinic in most general hospitals is deplored by Clarke, who insists that a closer cooperation between the mental hygiene service and the other departments is essential in a progressive institution. The system used at the medical school in Rochester, N. Y., is briefly described. The psychiatric clinic is well organized and the staff is adequate; it is used not only as a consultation service but as a primary clinic for the study and treatment of patients with behavior problems. Attached to the department are two schools, a nursery school for children from 2 to 5 years of age and a training group for children from 8 to 12. In the former school there is active cooperation between pediatricians and psychiatrists. Effort is made to treat the mother also. The older group of children presents more serious problems as a rule, and the program of training is individual, variable and interesting, with much emphasis on manual work. The psychiatric and pediatric services have established a clinic for patients with enuresis and have emphasized the correction of habits due to faulty training and the readjustment of unwholesome emotional situations. In all cases, staff conferences are held in which both departments take an active part. In a discussion of this paper, Robert McGraw warned against excessive enthusiasm on the part of child guidance clinicians and called attention to the possibility of their work being discredited by too much "ballyhoo" or by inability to produce the results claimed.

DAVIDSON, Newark, N. J.

CORRELATED ANATOMICAL AND PHYSIOLOGICAL STUDIES OF THE GROWTH OF THE NERVOUS SYSTEM OF AMPHIBIA: X. COROLLARIES OF THE ANATOMICAL AND PHYSIOLOGICAL STUDY OF AMBLYSTOMA FROM THE AGE OF EARLIEST MOVEMENT TO SWIMMING. G. E. COGHILL, J. Comp. Neurol. **53**:147 (Aug.) 1931.

This article is the tenth of a series of papers, the first of which appeared in 1914. During this period the author has continuously investigated the many aspects of the problems involved. The purpose of this paper is to present certain consequences of the work in its bearing on larger problems of neurology and behavior. The preceding papers have followed in great detail the changes in the structure of the nervous system from its beginnings until the time when the animal is able to swim. Many of these observations have been summarized in Coghill's lectures, which he was invited to give in London, at University College, in 1928, and which have been published under the title "Anatomy and the Problem of Behavior," by the Cambridge University Press. But the author does not wish these correlative studies of increasing complexity of structure and function to be accepted as an unqualified support of an extreme mechanistic interpretation of behavior on the basis of sensorimotor response. In the present paper he undertakes to show that there is also a structural basis for purely intrinsic factors of behavior, which connote spontaneity as a whole. The following topics are discussed: nervus terminalis, longitudinal mechanisms of association, commissural relations, cerebellum, cerebrum, polarization and direction of growth of neuroblasts, analysis and synthesis in the growth of the cerebrum, and centers of spontaneity.

ADDISON, Philadelphia.

OBSERVATIONS ON OCULAR PALSIES. GORDON HOLMES, Brit. M. J. **2**:1165 (Dec. 26) 1931.

The brevity and completeness of this discussion of ocular palsies make an abstract of it almost impossible. Ocular palsies are divided and considered under

three main and distinct classes: (1) paralysis due to disease of motor nerves or nuclei, (2) conjugate palsies and (3) supranuclear palsies. A differentiation is made between nuclear, stem and root palsies, indicating the most frequent causes of each. They are all characterized by paralysis of muscles. The term "conjugate ocular palsies" is usually applied to the loss of power of movement of the two eyes in any direction, provided this is not due to the chance association of paralysis of the prime movers of each eye. It occurs in lesions involving associative fibers between the ocular nerve nuclei and probably in the dorsal longitudinal bundles. The most common form is paralysis of lateral movements of the eyes to one side. When it is unilateral the patient is unable to look toward the side of the lesion. In supranuclear palsies the eyes fail to move in response to certain stimuli only. Voluntary movements may be impossible, yet the eyes will respond to stimuli from centers other than the cortex, as, for example, in response to labyrinthine stimulation. It may be elicited by having the patient fix on an object; on turning the head the eyes may remain fixed on that object.

FERGUSON, Niagara Falls.

TREATMENT OF GENERAL PARALYSIS. LELAND HINSIE and JOSEPH BLALOCK, *Am. J. Psychiat.* **11**:541 (Nov.) 1931.

In a study of 197 treated patients with dementia paralytica, the authors found improvement or remission in 40 per cent of the cases when malaria was used and in 42 per cent when tryparsamide was employed. The incidence of death was 43 and 45 per cent, respectively. On the other hand, combined treatment resulted in a death rate of only 19 per cent. However, patients who died after having received malaria treatment only would be classified as dying after treatment with malaria, whereas many of them would have received tryparsamide had they lived; hence combined treatment was administered to the more resistant group. In the absence of treatment, the average patient with dementia paralytica lives a year and a half in a hospital for mental diseases before death occurs. Treated patients have shown an average span of life (after treatment) of three and a half years for men and four and a half for women. The life expectancy of a patient treated with malaria is forty months after initiation of treatment, whereas the group treated with tryparsamide lived for an average of fifty-three months. Of the patients who died, a third of the males but only a seventh of the females had convulsions. Laboratory data show an increased tendency each year toward negative findings. The cell count is the earliest factor to reduce, the colloidal gold curve being the most stubborn.

DAVIDSON, Newark, N. J.

KORSAKOFF'S SYNDROME: ITS HISTOPATHOLOGY. E. ARNOLD CARMICHAEL and RUBY O. STERN, *Brain* **54**:189 (June) 1931.

If the term "Korsakoff" syndrome is to be used, it should be applied in the original meaning that Korsakoff ascribed to it. Toxemia is the essential factor in the production of the syndrome. The literature of pathologic investigations in cases of alcoholism is reviewed, beginning with the first pathologic record described by Korsakoff himself in 1892. Five cases of Korsakoff's syndrome associated with alcoholism were studied pathologically. The lesions in the brain were confined to the cerebral cortex and were incident on the cells; there was no tract degeneration such as had been found by other workers. The most remarkable feature was the widespread deposit of lipochrome material in the nerve cells and neuroglia cells in the cortex, which has been described only in pellagra. As the formation of excessive quantities of lipochrome is a disorder of cell metabolism, it is suggested that there is an exaggeration of the normal process of lipochrome formation. The chromatolytic changes are similar to those in "central neuritis" of Meyer, and in Pearson's study pellagra was the only disease in which chromatolysis of the Betz cells was present in every case. It is suggested that a common factor, which may be a "deficiency," which permits a toxin to exert its effects on the highly specialized nerve cells of the cortex may be present in both Korsakoff's syndrome and pellagra.

MICHAELS, Boston.

ACUTE POLIOMYELITIS IN SYRACUSE, NEW YORK. A. CLEMENT SILVERMAN, *Am. J. Dis. Child.* **41**:829 (April) 1931.

The epidemiology of infantile paralysis in the six outbreaks between 1916 and 1929 is reviewed by a clinical analysis of the cases occurring in Syracuse, N. Y., during that period. In every epidemic the male patients exceeded the female; in each outbreak about three fourths of the cases occurred in children under the age of 9 years. Negroes seemed less susceptible than white persons. August was the month when the greatest number of cases occurred. Evidence of the infectious nature of the illness was offered by studying maps showing the progress of the disease in Syracuse from day to day; foci would often spread to adjoining parts of the city. About half of the cases were of the spinal type, the remainder comprising both the bulbar and the combined forms. All of the patients who were treated received serum intraspinally. Somewhat less than 50 per cent escaped paralysis; this suggests that the serum was of some value, although in the absence of a control series it is not certain. Silverman favors the intraspinal injection of convalescent serum in preparalytic cases as a logical and harmless therapeutic procedure.

DAVIDSON, Newark, N. J.

ON NEURODERMATOMYOSITIS. S. LOEWENTHAL, *Schweiz. Arch. f. Neurol. u. Psychiat.* **28**:126, 1931.

The characteristic feature of the four cases of neurodermatomyositis here reported consisted in induration of the skin, subcutaneous tissue and muscle with marked tenderness on pressure over the parts involved. Pain was a prominent symptom, especially at the onset, and in some instances tenderness of the nerve trunks was demonstrated. In the first case, the symptoms were confined to one lower extremity and the forearms; the muscles of the involved leg were weak, and the achilles reflex was abolished. In the second and third cases the manifestations were confined to the lower extremities, and in the fourth case to the region of the deltoids and the inner surface of the thighs. The symptoms were rather suggestive of sciatic neuritis in the first three cases. After a brief review of the literature, Loewenthal expresses the view that dermatomyositis and the clinical complexes related to it represent a conglomeration of conditions, the causes of which are to be sought in a variety of endogenous and exogenous factors. So far as his cases were concerned, their chronic inflammatory character and the favorable response to heat and injections of vaccine suggested an infectious origin.

DANIELS, Rochester, Minn.

ENCEPHALOGRAPHY IN CHILDREN. MAXWELL BOGIN, THEODORE G. HOLZSAGER and BENJAMIN KRAMER, *Am. J. Dis. Child.* **42**:526 (Sept.) 1931.

This article on encephalography in children is of importance primarily because of the excellent bibliography that accompanies it. No new or unusual procedures or results are reported. The authors use the single lumbar approach and a needle with a three way stop cock; they proceed with roentgen examination immediately after the injection of the air. They report on 20 cases occurring in children, 7 of which are described in detail, and they tabulate their findings in 4 cases of meningococcus meningitis, 5 cases of cerebral maldevelopment, 2 of hydrocephalus, 2 of abscess of the brain, 2 of epilepsy, 2 of encephalitis, 1 of tuberculous meningitis, 1 of tumor of the brain and 1 case of congenital communicating hydrocephalus. They emphasize the fact that the procedure is not without danger, and report that several of their patients died following the injection and that others went into a condition of shock and required stimulation. The roentgen plates are very clear and demonstrate the great aid that encephalography may give in the differential diagnosis of many puzzling intracranial conditions and in the exact localization of these conditions in infancy and childhood.

LEAVITT, Philadelphia.

THE DIFFERENTIAL DIAGNOSIS AND PATHOGENESIS OF TUMOR-LIKE VASCULAR PROCESSES IN MIDDLE-AGED AND OLDER PERSONS. CARL F. LIST, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **134**:616 (July) 1931.

The differential diagnosis of a tumor of the brain from vascular diseases which may simulate it is difficult in older people because, first, the general signs of tumor of the brain, such as headache, choked disk and vomiting are less pronounced or are lacking, and second, cardiovascular diseases which may simulate tumor of the brain are frequent in these decades of life. List reports ten cases of cerebral vascular disease, especially with hypertonic and uremic symptoms, which clinically simulated true tumors of the brain. The cases showed similar histories, including papillitis, significant spinal fluid findings and even changes in the sella. In one case there was both intrasellar and suprasellar calcification, owing to a calcified internal carotid vessel. The differential diagnosis can be made only by means of encephalography or ventriculography, but these should be used only when operation is contemplated. Pathologically, the brains show nothing which cases of arteriosclerosis without tumor of the brain do not show. The changes in the optic nerve are not easily distinguished from true choked disk. They are due less to mechanical than to toxic causes.

ALPERS, Philadelphia.

GLYCOSURIAS OF CEREBRAL ORIGIN. CARL JULIUS MUNCH-PETERSEN, *Brain* **44**:72 (April) 1931.

From previous experiments it is probable that, besides the center for regulating sugar in the medulla, there are also centers in the hypothalamus and perhaps others in the corpus striatum and the cerebellum. In extrapyramidal disease, the expected increase of sugar in the spinal fluid following the injection of epinephrine is not encountered. The test itself is called the epinephrine-liquor-sugar-reaction. In seven cases in which the central nervous system was involved, the reduced epinephrine-liquor-sugar-reaction pointed toward localization in the extrapyramidal system. In view of the embryonic relationship of the hypothalamus and entodermal tissue, a functional relationship is suspected. With a patient having a suspected tumor in the superior corpora quadrigemina as a text, a complicated theory is advanced to explain the presence of the glycosuria, i. e., a disturbance of neurohypophyseal function which may cause a reduction in the absorbing power of the tubules of the kidney. A reversal of the situation is described in a patient with symptomatic diabetes insipidus, dystrophia adiposogenitalis and pulmonary tuberculosis — increase of the power of reabsorption. It would seem that more evidence is necessary before this speculation can be accepted.

MICHAELS, Boston.

THE SPINAL FLUID CYTOLOGY IN POLIOMYELITIS. H. E. THELANDER, E. B. SHAW and MARGARET LIMPER, *Am. J. Dis. Child.* **43**:1117 (Nov.) 1931.

The authors' work is based on the assumption that the cytology of the spinal fluid is of great importance in establishing a differential diagnosis between poliomyelitis and other diseases of the central nervous system, especially tuberculous meningitis. They present a graphic study of the cell counts and range of polymorphonuclear cells in 122 cases of poliomyelitis and a comparison with similar curves in 147 cases of tuberculous meningitis. In poliomyelitis they report a cell count of between 10 and 700, the greatest number of cases having shown between 50 and 200 cells. In cases with bulbar involvement, the spinal fluid cell count is relatively low. They report that in one half of their cases the percentage of polymorphonuclear cells was between 50 and 70, which is contrary to the usual findings. A concomitant blood count consistently showed a slight leukocytosis with a relatively high polymorphonuclear count. The poliomyelitis and tuberculosis curves parallel each other in nearly all particulars, the tuberculosis count generally being between 50 and 200 cells, the same as is noted in the cases of poliomyelitis. This study of the spinal fluid offers little of differential diagnostic value.

LEAVITT, Philadelphia.

## Society Transactions

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### NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

*Regular Meeting, Oct. 11, 1932*

BYRON STOOKEY, M.D., *Chairman*

#### HISTOPATHOLOGIC STUDY OF TWO ANGIOMAS OF THE BRAIN. DR. ABNER WOLF and DR. SAMUEL BROCK.

Pathologic studies of angiomas of the brain are comparatively rare in the literature. We have been fortunate enough to obtain pathologic material in one such case, the clinical and roentgenographic study of which was reported in a recent issue of the Bulletin of the Neurological Institute of New York by Dr. Brock and Dr. Dyke. In addition, Dr. Dandy has provided histologic material from another such tumor, which was seen by one of us.

The first case is remarkable in many respects. Histologically the tumor was a venous angioma, while clinically it presented some features of an arteriovenous angioma of the brain. An angioma in the retina of one eye extended back through the optic nerve and chiasm to the brain proper and was associated with an angioma of the cheek on the same side.

In Lindau's disease, hemangioblastomas of the cerebellum, brain stem or spinal cord, and of the retina and skin are found associated with nonangiomatous multiple cysts of the pancreas and kidney. Vascular malformations showing a similar distribution are rare. Heitmüller reported a case of arteriovenous angioma of the retina in which there were symptoms of an intracranial angioma, and Kreutz reported a case of arterial angioma of the retina in describing which he mentioned no intracranial lesions, but which, on review, seems to have been associated with one. Yates and Paine reported a case of venous angioma of the retina associated with an arteriovenous angioma. None of these cases was verified pathologically.

CASE 1.—The patient, a man, aged 21, had had a nevus on the right cheek from birth. At the age of 15 he had what seemed to be an attack of acute epidemic encephalitis, during which he slept continuously for six weeks; later he was delirious for a month. The upper and lower extremities on the right side became helpless, and speech was impaired. When seen at the Neurological Institute, six years later, he complained of defective speech, unsteady gait, a noise in the right ear of seven years' duration, fatigability and depression, with suicidal trends and mental deterioration.

On the right side of the face was a raised, soft, angiomatous lesion. The right ear pulsated synchronously with a marked throbbing of the right temporal and right carotid arteries. Over the temporal region a loud systolic bruit was heard; it extended down into the neck. Compression of the carotids suppressed the bruit and the tinnitus. There was bilateral exophthalmos, more marked on the right side, with bilateral weakness of the internal rectus. There was mimetic weakness of the face on the left side; speech was slow and somewhat scanning. There were cerebellar signs and mental deterioration. The right eye was blind, and ophthalmoscopic examination disclosed a venous angioma of the right retina, which almost completely obscured the disk. Some of the veins showed proliferation of connective tissue, indicative of organization following thrombosis.

Dr. Krug and Dr. Samuels made a special study of the right eye and optic nerve in this case and provided us with some of their material. There was an angioma of the right retina, the right optic nerve, the right side of the optic chiasm,

the right side of the midbrain, compressing the aqueduct of Sylvius and producing an internal hydrocephalus of the lateral and third ventricle, the right brachium conjunctivum and the right dentate nucleus of the cerebellum. Histologic examination showed a venous angioma. The vessels were large, irregular and thin-walled. They rarely showed any elastica, and there was no internal elastic membrane. The media showed only a few smooth muscle cells, arranged circularly and interspersed in the meshes of collagenous connective tissue. Between the vessels was nerve tissue which showed varying degrees of gliosis. As has been stressed by Cushing and Bailey, these vascular malformations differ from true neoplasms of vascular origin in that brain tissue is found between the vessels.

It was evident from histologic examination that anatomically the angioma was of the venous type. This was substantiated by microscopic examination of material from the eye, the optic nerve and the brain. The fact that the patient had a trigeminal nevus was in accord with this diagnosis. Cushing and Bailey said: "So far as we are aware, no arterial angioma of the brain has been reported in association with a trigeminal nevus." On the other hand, venous angiomas are never accompanied by exophthalmos and pulsation of the carotids, nor do they show an intracranial bruit. In our patient the first two symptoms were present, and a cranial bruit was observed. It has been pointed out, however, that in venous angiomas a communication may at some time develop between one of the venous channels and a nearby artery. In this case a bruit appears, and symptoms of arterial angioma, such as exophthalmos, pulsating and enlarged carotids and a hypertrophied heart, may eventually appear. The walls of the veins near the site of the communication undergo a change, developing an internal elastic membrane and becoming arteriolized. We are inclined to class the case as a venous angioma in which an arterial communication was established, and which would eventually have shown the histologic, as it did some of the clinical, features of an arteriovenous angioma.

CASE 2.—The patient, a man, aged 34, had had an acute illness ten years before, which was characterized by headache, dizziness and vomiting. He was kept in bed for three or four months. The diagnosis was acute epidemic encephalitis. He showed sluggish pupils, weakness of the left internal rectus, nystagmus, bilateral ptosis, paresis of the right side of the face, diminution of the deep reflexes in the upper extremities, absent reflexes in the lower extremities and retention of urine. He recovered and seemed well for nine years, when he suddenly lost consciousness. Similar attacks followed during the year, accompanied with convulsions. After a number of convulsive seizures had occurred in rapid succession, he came to the clinic. At this time he showed bilateral papilledema, with optic atrophy, left homonymous hemianopia, paralysis of the left internal rectus, nystagmus, facial weakness on the right side, diminution of deep reflexes and peculiar sensory and mental changes. He was discharged from the hospital and was later admitted to the Johns Hopkins Hospital under the care of Dr. Dandy. Ventriculography revealed internal hydrocephalus. An operation was performed. The patient died. Dr. Dandy reported: "Post-mortem findings in the case of M. D. showed that he had an angioma filling the upper third or fourth of the midbrain in the region of the quadrigeminal bodies. It extended entirely across this part of the brain stem." We were permitted to study some of Dr. Dandy's sections. The vessels of the angioma varied considerably in size and showed an unequal development of layers. In many instances there was a nodular overgrowth of the intima; in some this was more diffuse, partially obliterating some of the vessels. There was imperfect formation of the media, with a tendency to form leiomyomatous nodules. The elastica showed an unequal development, but in most instances an internal elastic membrane could be detected. Many of the vessels showed aneurysmal out-pocketings. Between the vessels gliosed tissue of the midbrain could be seen. At the margins of the lesion were capillary channels which showed proliferation of the intimal lining; these were regarded as a possible indication of continued activity of the tumor.

**EXPERIMENTAL TOXIC ENCEPHALOMYELOPATHY: DIFFUSE SCLEROSIS FOLLOWING SUBCUTANEOUS INJECTIONS OF POTASSIUM CYANIDE. DR. ARMANDO FERRARO.**

In order to elucidate the etiology of some degenerative pathologic conditions, I have undertaken experimental studies of the action of potassium cyanide on the central nervous system. Cyanide is a product of intermediary metabolism and seems to be a precursor of urea and perhaps of creatine. According to Warburg, it affects the respiratory enzymes and therefore inhibits the respiration of tissue. I thought therefore that interference with the supply of oxygen might, through inappropriate metabolism, lead to the destruction of elements, with the consequent production of multiple or diffuse sclerosis.

Potassium cyanide was injected subcutaneously into fourteen cats and four monkeys, the minimum dose of 2 mg. being increased daily by 0.5 mg. until a maximum dose of 35 mg. daily was reached in one of the animals. Following each injection, the following clinical symptoms resulted: increase in the respiration rate, in proportion to the amount of medicament injected; vomiting; bowel movement; twitchings, localized or generalized; occasional tremors of the head; occasional nystagmus; spasms, hyperreflexia and spasticity of the legs. Following repeated injections, a spastic paralysis of the hindlegs developed, which was, however, transitory, lasting from a few hours to a few days; it was found that if the injections were not discontinued, the paralysis might remain stationary; blindness occurred, which also seemed to be transitory and there were generalized convulsions, which at times proceeded from a single convulsion to a status epilepticus.

From a histopathologic standpoint the lesions consisted in a diffuse process of demyelination involving indiscriminately all areas of the white substance, the process being, however, more pronounced in the frontal and occipital regions. The process was particularly severe in the corpus callosum and in the periventricular regions. The brain stem and the cerebellum were also the seat of demyelination, especially the parts surrounding the fourth ventricle. The process of demyelination extended to the optic nerve and the optic chiasm, where isolated or diffuse patches of the lesions were often found. The axis cylinders suffered degeneration, which sometimes proceeded from a moderate stage to one of more or less complete disintegration. Of the neuroglial elements, the astrocytes at the periphery of the areas of demyelination disclosed considerable progressive changes, both hypertrophic and hyperplastic. Progressive changes of the same elements were also present in some areas of demyelination in which the destructive process was not pronounced. The fibrous neuroglia showed also considerable reaction of a progressive type in correspondence with the areas of demyelination, and with the Holzer method for staining glial fibers a marked process of gliosis was detected in correspondence with the areas of demyelination. Microglial and oligodendroglial elements showed progressive and regressive changes and a tendency toward the formation of compound granular corpuscles. The blood vessels did not show embolic or thrombotic changes, but in some areas they disclosed a definite swelling of the endothelium. In rare instances, endarteritic changes of the progressive type were found.

Sixteen of the eighteen animals presented no inflammatory changes, the process being a typically degenerative one. The blood vessels in these cases appeared to be surrounded by proliferated elements, the majority of which were compound granular corpuscles. Only two dogs showed definite lesions which would satisfy the classic requirements of inflammation.

In addition to the areas of demyelination there were areas of necrosis, in which all the elements had undergone degenerative and destructive changes. In the more severely damaged areas there were softenings, sometimes of considerable extension. It was only in the areas of softening that mesodermic connective tissue seemed to be spreading and, together with the neuroglial elements, to be proceeding to repair. The softenings were not, however, the main histologic feature nor did they show a predilection for the striatum, as A. Meyer found in the case of dogs.

In the cortex in most cases there were no appreciable changes in the sense of diffuse necrosis or softening. Only occasionally were small areas of softening present; more often there was a diffuse involvement of the nerve cells, which underwent the severe type of degeneration of Nissl. Occasionally large areas of nerve cells appeared diffusely shrunken.

In the spinal cord, primary areas of demyelination were present throughout the cross-section, though they were most frequent in the posterior columns. The fibroglial reaction was not pronounced in the spinal cord, and no areas of softening were encountered.

I think that the pathologic process which was reproduced experimentally can practically be superimposed on the pathologic changes in diffuse sclerosis. The relationship between diffuse and multiple sclerosis favors the unity of these two clinical conditions. I have no complete explanation for the occurrence of inflammatory lesions in two of the eighteen cases. I believe that many conditions labeled clinically with various names may ultimately be reclassified within the boundary of diffuse sclerosis, as encephalomyelopathy or encephalomyelitis, with the additional qualification of an etiologic factor. I believe also that possibly the conception of diffuse sclerosis as a clinical entity must be abandoned, and that the condition must be considered as a syndrome or an end-result of various pathologic conditions, among which both original general infections and toxic processes may play an important rôle.

#### DISCUSSION

DR. FOSTER KENNEDY: Dr. Ferraro's work has thrown some light on cases which are put rather loosely in the clinical domain of insular sclerosis. I have resisted the temptation to enlarge the scope of insular sclerosis. There is a tendency to throw under that cloak a number of scattered and rather amorphous clinical groups.

DR. RICHARD M. BRICKNER: I wish to comment on one point to which Dr. Ferraro alluded, namely, the prevailing dispute as to whether diffuse sclerosis, multiple sclerosis and encephalomyelopathy are the same disease or whether they are different processes. Work of the nature of Dr. Ferraro's will probably do more toward solving this question than all the debating we can do. If enough different substances are used to produce patchy demyelination in animals, this question will solve itself, and it would be well to postpone discussion until it is so automatically solved.

Some of Dr. Ferraro's findings differ from the orthodox pathologic conditions found in multiple sclerosis. Areas of softening are rare in that disease. However, I think that it is more important to stress similarities than to pick out minor differences. The animals with diffuse inflammatory lesions in the brain perhaps do not belong in the same group as the other animals, and the findings in their cases should not vitiate the results. I do not think that it matters much whether the picture obtained resembles multiple sclerosis more than it does diffuse sclerosis, or vice versa. The important point is that it has now been demonstrated that myelin can be caused to disintegrate by the injection of an extrinsic, non-infectious agent. One is no longer called on to explain these changes by something inherent in the myelin itself. The work of Putman and his collaborators, which was presented before the section last year, tends in the same direction. The employment of still other substances to produce demyelination in vivo will undoubtedly provide valuable information from the standpoint of the disintegration of myelin.

Valuable as this work is, I am of the opinion that final knowledge of the causes of these various diseases will not be obtained until one can produce typical lesions by introducing products from the bodies of patients suffering from such diseases. When injection of the urine, spinal fluid or some metabolic product from patients suffering from diseases of demyelination causes a reproduction of the pathologic picture, then only will definite etiologic knowledge be available. Another feature of significance is that regeneration of myelin in the central nervous

system, while its occurrence has been suspected, has never been demonstrated, so far as I know. Some of Dr. Ferraro's animals recovered from paralysis of the hindlegs, and the supposition is warranted that in these instances myelin regenerated. Potassium cyanide might be employed as an agent for the graded destruction of myelin, preparatory to studies of the regeneration of myelin in the central nervous system.

DR. ISRAEL STRAUSS: In line with what Dr. Brickner and Dr. Kennedy have said, I consider this to be an extremely important piece of work. As Dr. Brickner has stated, Putnam and his associates, using tetanus toxin, have also produced demyelination. I think, however, that Dr. Ferraro's work has gone a little farther. As to solving the problem of multiple sclerosis, diffuse sclerosis, encephalomyeloradiculitis and all the related diseases by work of this kind, Dr. Ferraro stated that he has not attempted to do any such thing. He has shown clearly that an exogenous poison can produce changes in an animal similar to those customary in these conditions. I do not recall having seen an area of softening or necrosis in a case of multiple sclerosis (I am not speaking of so-called acute multiple sclerosis); this may mean only that with this particular toxin the process is more intense than in disseminated sclerosis in human beings.

In two of Dr. Ferraro's cases there was an inflammatory reaction. Cases have been reported in the literature, and I have seen one at the Montefiore Hospital, in which in multiple sclerosis of long standing there were evidences of inflammatory reactions—perivascular infiltration, exudation, etc. The question arises: Is this part of the slow degenerative process or is there an invasion of the nervous system by a virus which produces the acute picture? Until the nature of the virus is discovered, one cannot answer that question. As Dr. Ferraro said, there may have been a secondary inflammatory invasion which it was not possible to detect. On the other hand, so-called inflammatory reactions may occur in degenerative diseases without the presence of an infectious process. One returns to the old question: What is an inflammation and what is a degeneration? I do not know of any one who has solved it. What does an infectious process do to the body? The presence of the bacterium is not the cause of the disease; it is the toxin, endogenous or exogenous, in the bacterium which causes the changes. Why cannot some other poison in the body cause the change which is called, from a narrow point of view, an exudation or infiltration?

On the other hand, disseminated sclerosis is a slowly developing process. I have no faith in the diagnosis of acute multiple sclerosis, unless by that is meant a typical multiple sclerosis syndrome which starts more or less acutely. All the cases in the literature described as acute multiple sclerosis in which high temperature, disseminated symptoms and inflammatory changes in the nervous system occur, are, in my opinion, not of the same type as ordinary clinical multiple sclerosis.

Dr. Globus and I recently studied a case, which will be reported in the Libman Memorial Volume, in a woman in whom symptoms developed within two months that I thought at one time were those of encephalomyeloradiculitis, and at another time multiple sclerosis. Because the symptoms developed within two months I called the condition acute multiple sclerosis, or, as I should have said, an acutely developing multiple sclerosis. Unfortunately the patient died after an injection of arsphenamine, with hemorrhagic encephalitis. In the cord and brain stem were perfect patchy areas of demyelination. When one studied the material, there was no evidence of an inflammatory lesion—nothing that would ordinarily be called inflammatory—but the perivascular spaces and the areas of demyelination were crowded with compound granular corpuscles loaded with fat. In other words, the case was one of a noninflammatory toxic reaction like that reported by Dr. Ferraro in his experiments. I believe, as Dr. Brickner stated, that the nature of these different diseases will not be solved until an infectious etiologic agent, a virus or a toxin, is found which, as Dr. Ferraro has shown, can produce this picture. Such a toxin, in my opinion, must be endogenous; where it is formed is the question. I do not believe that it will be found in the urine, the spinal fluid or the excreta of the body. It will be formed somewhere by the intermediary metabolism of the patient.

DR. PAUL SCHILDER: It is important that, as in the experiments of Dr. Ferraro, one can produce a picture that corresponds closely to that of diffuse sclerosis, or, as I should prefer to say, of encephalitis periaxialis, by the introduction of an exogenous factor. The picture which Dr. Ferraro has demonstrated is certainly much more like diffuse sclerosis than like multiple sclerosis. In the discussion it has been mentioned that patches of softening are unusual in multiple sclerosis. They are almost typical for the picture of diffuse sclerosis. The manner in which the corpus callosum is affected is also typical. This case corresponds closely to the pictures in diffuse sclerosis, so that the similarity is almost complete. There is only one difference: in diffuse sclerosis one does not find the extensive lesions which seemingly progress from one spot to adjacent parts.

It has been said that it is of no importance that two cases showed inflammatory changes. I do not think that that statement is justified. In some of my cases I have observed clearcut inflammatory changes in the histologic picture. Furthermore, it is not correct to say that there is a strict division between inflammatory and degenerative processes when there is an exogenous factor in the disease; the same factor can provoke both. I think, therefore, that these two cases are of special importance.

DR. FERRARO: As Dr. Schilder has said, one does find areas of softening more commonly in diffuse sclerosis than in multiple sclerosis. Through areas of softening are not common in multiple sclerosis according to the literature, they have been discussed in a number of reports, especially in cases of so-called acute multiple sclerosis, or, as Dr. Strauss said, cases of multiple sclerosis running a rapid course. Not only have areas of softening been reported in acute cases but, according to Wohlwill, they were found in an old case of multiple sclerosis, and the areas were correlated by the author with a possible exacerbation of the process. In my experiments, the histopathologic picture certainly bears a greater resemblance to diffuse sclerosis than to multiple sclerosis.

Concerning the inflammatory reaction in two cases, I do not think that it is of no importance. It is important, especially because it proves that inflammatory conditions may develop under the stimulus of purely toxic factors. I am at a loss, however, to explain its occurrence. Altogether, I think that the experimental encephalomyelopathy which I have reproduced is essentially a degenerative toxic process; an explanation of the occurrence of inflammatory manifestations must await more advanced pathologic knowledge.

I am perfectly in accord with the conception that, in building up clinical entities, one must always bring together and harmonize the clinical and the pathologic criteria, though I would like to add another criterion, the etiologic one. Clinical entities might therefore be built on at least three elements: the clinical, the pathologic and the etiologic. It has been precisely in an attempt to search for the third factor, the etiologic one, still unknown in cases of diffuse and multiple sclerosis, that my experimental work has been done. All that I can say is that lesions, the pathology of which is identical with that of diffuse sclerosis, can result from the use of an exogenous toxic substance which in this particular instance (cyanide) represents also a product of intermediary metabolism. Through a combination of the clinical, histologic and etiologic factors there will gradually be acquired a clearer conception of entities which, like diffuse and multiple sclerosis, are still but vaguely understood.

CLINICAL AND PATHOLOGIC NOTES IN TWO UNUSUAL CASES OF TUMOR AT THE  
BASE OF THE BRAIN. DR. E. D. FRIEDMAN and DR. LEWIS D. STEVENSON.

This paper is to be published in full elsewhere.

PERICAPILLARY ENCEPHALORRHAGIA FOLLOWING THE ADMINISTRATION OF  
ARSPHENAMINE. DR. JOSEPH H. GLOBUS and DR. SOL. W. GINSBURG.

This paper is to be published in full elsewhere.

## PHILADELPHIA NEUROLOGICAL SOCIETY

Nov. 25, 1932

A. M. ORNSTEEN, M.D., *President, in the Chair*

## POSTEROLATERAL SCLEROSIS FOLLOWING MASSIVE HEMORRHAGE. DR. A. TORNAY and DR. R. HOLTZHAUSER.

This patient, aged 40, is presented because of the unusual occurrence of posterolateral sclerosis following massive hemorrhage.

*History.*—The present illness began following the birth of a child on March 1, 1927. Labor was difficult and prolonged. The baby was born by a breech presentation following instrumentation, first without anesthesia and later with ether. The patient was told that much blood was lost and that clots had to be cleaned up with a shovel and a dust pan. The patient's condition was so poor during delivery that a priest was called. On the second day after delivery she felt cold all over. Toward the end of the second day, the sensation of cold settled in the legs; the patient said that the legs felt as if they were covered with a wet, cold sheet. For the first week after delivery she could not distinguish her children by sight; all objects appeared blurred. The condition gradually improved, and the patient was kept in bed for three weeks. When she attempted to sit up in a chair, she fainted. She was able to walk in the fifth week after delivery. At that time she was unable to tell where her feet were and had to watch where she placed them. She became bewildered in traffic and always had to have someone lead her. Incontinence of urine began four months after delivery and spasticity of the right arm, with acute flexion at the elbow, in November, 1927. This condition gradually improved. The condition of the legs became worse by degrees, with occasional periods of slight improvement. She has now been bedfast for four months.

*Examination.*—On Nov. 15, 1932, Dr. Hadden found the pupils equal and reacting normally to light and in accommodation. A suggestion of slight nystagmus was present on extreme lateral deviation. Power in the upper extremities was good and approximately equal on the two sides. The finger-to-nose test was badly done with the left arm, but fairly well with the right. The left lower extremity showed a marked flexor deformity. There was little power in the right lower extremity, but it could be completely extended. The patellar reflexes were not elicited. There were sustained ankle clonus on the right and a bilateral Babinski sign. Reflexes of defense in the lower extremities were marked. Hoffman's sign was positive bilaterally. The abdominal reflexes were absent. Sense of pain was present throughout. Senses of position and vibration were apparently absent in the lower extremities. Vibration was recognized in both upper extremities. In the left hand, sense of position and sensation were definitely impaired. Astereognostic sense was lost.

Blood counts revealed: hemoglobin, 65 per cent; erythrocytes, 4,310,000; leukocytes, 5,840, with polymorphonuclears, 70, transitionals, 5, lymphocytes, 23, and eosinophils, 2 per cent. The color index was 0.75. Three counts gave approximately the same results. The reticulocytes averaged 2 in 1,000 red cells. Gastric analysis showed the presence of free acid in all specimens, slightly in excess of that normally present. The Wassermann reactions of the blood and spinal fluid were negative. Chemical studies of the blood revealed nothing of importance. The urine was normal. In the spinal fluid, globulin and sugar were normal; cells numbered 75, and red blood cells were present; smears and cultures gave negative results; the result of the colloidal gold test was 555432000000. Examination of the stools gave essentially negative results, no ova or parasites being found.

Physical examination revealed that the patient probably had a sinus disease, and this was borne out by roentgenograms, which demonstrated maxillary sinusitis on the right side. Examination of the eyegrounds gave negative results.

## DISCUSSION

DR. SAMUEL B. HADDEN: Dr. Tornay said that the features of interest in this case are not the neurologic findings but the events which preceded their onset. From the description of the delivery given by the patient, there can be little doubt that there was massive hemorrhage. The patient's description of her symptoms shortly after delivery is classic. She had difficulty in walking because she could not feel the ground beneath her feet, did not know the position of her feet and found it necessary to watch the floor or ground while walking. For a period of three weeks vision was so impaired that she could recognize the members of her family only by their voices. Unquestionably there was almost immediate serious impairment of the nervous system. It is difficult to establish the existing pathologic changes in such a case at the time of onset. It is my belief that the anemia results in anoxemia, which predisposes to edema. If this state continues sufficiently long, permanent damage may result. As a part of the anoxemia, the nerve-endings may suffer, with the gnostic types of sensation suffering the most. After the anoxemia is corrected, the symptoms may rapidly disappear. A few months previous to presentation I saw a patient in Dr. Cadwalader's service in whom this occurred. The symptoms of posterolateral sclerosis with impairment of vision, with onset following a massive uterine hemorrhage, disappeared rather quickly after transfusion.

In the case presented by Dr. Tornay, the patient definitely dated her symptoms from the time of delivery; they have progressed rather slowly since. She presents none of the symptoms of pernicious anemia. A mild sinus disease existed, which may be a contributing factor. The colloidal gold test shows a rather typical alteration in the first zone, which is suggestive of multiple sclerosis, but the syndrome is that of typical posterolateral sclerosis; I consider it to be of the anemic type, with onset after massive hemorrhage.

DR. JOSEPH McIVER: Twelve or fifteen years ago, while I was an assistant to Dr. James Hendrie Lloyd, a patient at the Philadelphia General Hospital had symptoms and signs of posterolateral sclerosis. After gastric analysis and a thorough study of the blood had been carried out, it was discovered that the patient had recently suffered from a severe hemorrhage due to hemorrhoids. According to his account, he lost about 1 pint of blood on one occasion and smaller amounts at other times. The condition of the blood was that of secondary anemia. There was no indication of pernicious anemia. At autopsy, microscopic sections of the spinal cord showed a posterolateral sclerosis of the type that is usually associated with pernicious anemia.

## A CASE OF OCCLUSION OF THE SYLVIAN ARTERY. DR. F. C. DOHAN.

*History.*—This case is presented because of the unusual symptomatology: a pure motor aphasia. The patient was her normal, good-natured self until about the first week in October, 1932. Then she complained of headaches. These disappeared in a few days, and it was not until the third week in October that she showed any difficulties in speech. The first aphasic tendency was that of being unable to say the addresses of places to which she wished to go. The aphasia became progressively worse until it reached its height during the first week of November.

The husband, a sister and a neighbor say that the patient has been able at all times to perform her household duties, to dress and to take care of herself. At no time were there peculiarities in the movements of the arms or legs, but there was something unusual about the mouth which seems to have been indescribable. To her associates she seemed to understand everything that was said to her. She was frequently seen apparently reading a newspaper, an undertaking which under the best of circumstances she had done with some little difficulty. At this time she had no need to write her name, which was the extent of her ability in writing. Her signature written at the hospital is said by her husband to be practically normal.

During this period the patient's emotions seemed to be somewhat less under her control than normally. She would frequently cry, saying, "I'll die." At other times laughter came as quickly and as easily as weeping.

Dr. A. M. Ornsteen saw the patient on November 8. At that time the right arm and leg were weaker than the left; the right plantar reflex was of the extensor type, and other findings were present as at the time of admission.

*Examination.*—On November 9, she was admitted to the University Hospital in the service of Dr. Spiller. The patient, an Irish-American woman, aged 52, was cooperative, oriented and good natured. The blood pressure was 150 systolic and 95 diastolic; later, it was 175 systolic and 100 diastolic. The heart, lungs and abdomen were essentially normal. The following neurologic observations were made: Ocular convergence was poor, and there was possibly some inability of conjugate deviation to the right. The pupils were normal except for slight sluggishness to light. There was weakness of the right side of the mouth. The right hand grip was 45, and left, 60 (the patient is right-handed). All tendon reflexes were more active than normal, but with no marked inequalities. Clonus, Babinski sign, Hoffmann sign and abdominal reflexes were not elicited. Sensation throughout the body was probably normal.

Examination of the speech revealed an inability of the patient to express herself. When asked to give her name she replied, "I cannot say it" without any interruption or difficulty. When asked if it was Monahan, she promptly replied in the affirmative. While spontaneous thoughts could not be expressed, she repeated phrases of not more than a few syllables clearly. When she reached the fifth or sixth syllable, she hesitated and was unable to find the word. Simple commands were carried out well; complex ones were not. Printed letters were understood and read. She spelled and pronounced her name. She was either unable or unwilling to sing; she could not write, although other skilled acts, such as approximating the thumb and fingers and picking up a pin were well performed.

A roentgenogram of the skull was declared by Dr. Pendergrass to show no evidence of a tumor of the brain, there being atrophy of the dorsum sellae such as is not infrequently seen in arteriosclerosis. Dr. Fewell, in an ophthalmoscopic examination, found the arteries of the fundi markedly sclerotic, with a corkscrew vein just above the margin of the left disk. The margins of the disks were clear. Dr. Behney diagnosed the condition as leukoplakia of the vulva, but found no evidence of true malignancy in the pelvis. Estimation of blood sugar, the Wassermann reaction of the blood, blood counts and urinalysis revealed nothing abnormal.

*Comment.*—Looking for sources of possible emboli, one finds no clinical evidence of cardiac lesions, pelvic thromboses or an infected wound, but the superficial vessels of both legs show marked sclerotic changes.

The patient was discharged from the hospital on November 22. Marked improvement in speech was noticeable. While making an examination for discharge it was found that she could say some of her usual prayers with accuracy and alacrity.

The aphasia and some of the more pronounced objective neurologic signs have improved remarkably. At the last examination, on Nov. 21, 1932, the patient had no Babinski sign, no marked weakness of the right arm or leg, much better right conjugate ocular deviation and better convergence, as well as only slightly overactive tendon reflexes.

#### CERVICAL TUMOR OF THE CORD WITHOUT SENSORY SYMPTOMS. DR. F. C. GRANT.

Tumors of the spinal cord not infrequently have an unmistakable clinical history. However, it is not uncommon for the symptoms they produce to be so unusual that the diagnosis of tumor is difficult to make. One of the principal symptoms by which the level of a tumor of the spinal cord may be determined is sensory loss. In the case that I shall report, the sensory loss was unusual in distribution, and the onset of the clinical picture and the distribution of the neurologic signs were peculiar.

*History.*—C. O., a white boy, aged 19, who was admitted to the University Hospital on Nov. 7, 1932, noticed about Oct. 1, 1932, that his neck was stiff. He also had a slight cold in his head. The stiffness increased, and pain on motion of the neck became severe. Two or three days later, he noted some weakness in the right arm. Within the next week the right arm and hand began to feel as though asleep and finally became almost completely paralyzed. About forty-eight hours after the right arm became paralyzed, the left arm became involved and within a week was paralyzed. There was no paresthesia in the left arm. At no time were there any disturbances of touch or other sensation in either arm; the right arm felt merely as though it was asleep. Owing to the time of year and the development of symptoms following a cold with stiffness of the neck, a diagnosis of anterior poliomyelitis was entertained. During the next six weeks the boy was in bed; he gradually lost power in the legs, the left leg being much more involved than the right. There was never at any time loss of sphincter control or any of the ordinary sensations in any part of the body.

*Examination.*—On admission the boy was poorly nourished and semistuporous. The head was held exactly in the midline and stiffly erect, because any movement of it caused intense pain in the neck and between the shoulders. He was completely paralyzed in both arms and in the left leg. He had power to flex and extend the right leg weakly at the thigh, knee and ankle. The reflexes in the left upper extremity were hyperactive; on the right these were normal. The reflexes were hyperactive in both lower extremities, more so on the left than on the right side. There was a pronounced and well sustained ankle clonus on the left and an abortive ankle clonus on the right; there was a patellar clonus on the left but not on the right. The Babinski sign was positive in the lower extremities, and the Hoffman sign in the upper extremities.

The cranial nerves were normal except for bilateral weakness of the eleventh nerve. There was no pupillary disturbance. There were no tremors, either about the face or in the extremities.

Sensory changes included complete anesthesia to touch and pain in the distributions of the second, third and fourth cervical roots on the left. There was vibratory loss on the left side up to the clavicle. There was loss of sense of position in the left hand, but not in the left foot. Sphincter control was normal. The patient knew when the bladder or rectum was distended, and his control of these functions was complete.

Roentgen examination of the head and cervical spine gave negative results. A lumbar puncture, with a Queckenstedt test, showed a complete block, with  $2\frac{1}{2}$  units of total protein on the first tap. The Wassermann and colloidal gold reactions were negative. There were 5 white blood cells and 40 red blood cells in the spinal fluid. The fluid was xanthochromic. Combined lumbar and cisternal punctures revealed a normal reaction in the cisternal manometer but no movement in the lumbar manometer on pressure over the jugular veins. Comparative estimation of total protein showed 15 units of protein in the spinal fluid and  $\frac{1}{10}$  unit in the cisternal fluid. To clinch the location of the tumor, chloriodized oil was injected into the cistern, and a roentgenogram was taken with the patient in the erect posture; it revealed a block at the level of the first cervical vertebra.

*Operation.*—Laminectomy, with removal of the upper five cervical spines and transverse processes, was performed. The dura was well distended; when the dura was opened, the tumor was found to involve the left side of the cord, posterolaterally, from the first to the fifth cervical segment. The tumor lay beneath the arachnoid and probably beneath the pia, and the upper four cervical roots on the left were stretched tightly over the tumor mass. The tumor was removed by dissection. This left a large cavity in the substance of the cord, which was reduced to a thin ribbon pushed anteriorly and to the right.

*Course.*—The boy has made an uncomplicated recovery and is regaining power in the right hand and right leg. Sphincter control was not disturbed by the extirpation of the tumor.

*Diagnosis.*—The pathologic diagnosis of the tumor, as reported by Dr. Alpers, was glioma.

*Comment.*—It seems to me extraordinary that a tumor of this size could have produced symptoms so suddenly, and that, occupying the position it did and compressing the cord to the extent revealed at the operation, it did not produce more marked sensory disturbances. I expected to find a tumor anterior to the cord, involving particularly the pyramidal tract. The tumor was apparently situated in a proper position to interrupt the fibers running in the tracts of Goll and Burdach, yet no definite sensory disturbances, except those due to involvement at the root, were present.

#### DISCUSSION

DR. TEMPLE FAY: This case not only indicates the difficulties in diagnosis but represents a successful surgical removal of a large intramedullary lesion. I recall a somewhat similar case at the Episcopal Hospital, the patient being under the observation of Dr. George Wilson. A girl, aged about 18, left home for work in the morning and first noticed difficulty in stepping up to the lower platform of the trolley car. After she had been seated in the car less than one hour, she attempted to get up, but found that the legs were so weak that she had to allow herself to be assisted from the car. She was admitted to the hospital two days later; the paralysis in the lower limbs progressed rapidly. Dr. Wilson at first could find no sensory disturbances and no distinct level of localizing value; a vasomotor sign was demonstrated in the third to fifth thoracic dermatomes. Within a few days, the patient began to have vague disturbances in vibration and sense of position, but no pain. A spinal block was demonstrated, and laminectomy was performed about two weeks after admission. Operation disclosed a huge intramedullary lipoma; no definition of the tumor was obtained. It was impossible to determine where the tumor began and the substance of the cord remained. The patient died, approximately six weeks after the operation, from pyelitis. The spinal cord was removed, and Dr. Winkelman examined the tissue. The tumor involved the entire thoracic cord.

It seems evident that function was maintained by fibers which remained intact, as has been described by Dr. Spiller in cases of glioma of the brain. The tumor had probably been present for a considerable time prior to the onset of symptoms, and the symptoms were in no way proportionate to the size of the tumor. Thus, as in Dr. Grant's case, an extensive lesion of the cord without classic symptoms was encountered. That function may persist in the presence of a tumor of such size, is of distinct interest.

DR. A. M. ORNSTEEN: Dr. Spiller and I saw a patient in whose case an intramedullary glioma was found. The patient stated that he had had no symptoms until on attempting to do a "back-flip" from a diving board, he noticed that he could not feel the edge of the diving board with the right foot, though he was conscious of the position of the left foot in its normal spatial relationship. From that moment he was conscious of paresthesia in the right foot, with gradually progressing monoplegia. The sudden onset of symptoms in tumors of the brain is perhaps better known than that in tumors of the spinal cord.

DR. F. C. GRANT: From the surgical point of view, the tumor, curiously enough, considering its pathologic type, was dissected easily from the surrounding cord. As soon as one large vein was ligated and the arachnoid sectioned, the tumor began to extrude. At the upper end of the tumor was a cystic area containing 5 or 6 cc. of yellowish fluid. Owing to the position of the tumor, I feared the possibility of respiratory collapse due to bilateral involvement of the phrenic nerve, although preoperative roentgenographic studies had shown normal diaphragmatic movement. Fortunately, however, nothing of the kind occurred. Convalescence was uneventful, and at discharge the patient was regaining much power in the right extremities and was beginning to move the left toes.

## CONTROLLED SPINAL ANESTHESIA; ITS VALUE IN ESTABLISHING APPROPRIATE LEVELS FOR CHORDOTOMY. DR. TEMPLE FAY and DR. NICHOLAS GOTTEN.

In order to study certain clinical problems of intractable pain, we have devised a simplified method for producing spinal anesthesia and controlling the anesthetic in such a way that the spinal segments and roots anesthetized can be determined in an orderly and progressive manner. The value of the test lies in establishing the highest level at which pain fibers enter the spinal cord from a given part. We have observed that deep vascular pain and pain due to pressure are not objectively or subjectively removed until the spinal roots have been anesthetized at levels higher than the peripheral nerve pattern would indicate. In order to obtain complete anesthesia in the lower extremities, it was necessary to raise the level of anesthesia to the third thoracic segment. We have observed that vascular types of pain persisting in an area of anesthesia on the face after obliteration of the trigeminal root are relieved by spinal anesthesia carried to the fifth cervical segment. We believe that the test is of value in determining the appropriate level for chordotomy, so that section of the anterolateral column can be accomplished sufficiently high in the spinal cord to include all pain fibers from the part involved. We believe that a distinct system of pain fibers may be carried along the large vascular structures to find entry into the upper thoracic cord, and that chordotomy must be done above the third thoracic segment in order to obtain total analgesia in the lower extremities, and as high as the fifth cervical segment when this type of pain occurs in structures of the upper portions of the body, including the face.

The patient is placed on a tilted table, with the head down and the body at an angle of at least 30 degrees; a spinal needle is introduced into the fourth or fifth lumbar interspace, and a similar needle into the cisterna magna. The cisternal needle is connected by a sterile rubber tube to a graduated buret containing 50 cc. of sterile physiologic solution of sodium chloride. As the buret is raised above the level of the lumbar needle, fluid flows from it into the cisterna magna, forcing spinal fluid out of the lumbar needle. The buret is then lowered to a level just below the lumbar needle, permitting the fluid to flow back into the buret and allowing air to be drawn into the lumbar needle. As the column of spinal fluid descends, 1 cc. of an ascending type of spinal anesthetic is then introduced into the lumbar needle, and this is gradually drawn down the spinal canal, segment by segment, by lowering the buret, so that the column of fluid in the buret comes to an equilibrium with the column of spinal fluid at the desired level indicated by the accepted physical landmarks on the back of the patient, as shown in the accompanying figure.

Objective and subjective tests may be carried out while the anesthetic is thus at will arrested at the level under consideration. The spinal anesthesia may be drawn down to the fifth cervical segment and checked at this point to prevent paralysis of the motor supply to the diaphragm, which may impair respiration and which is undesirable. On the other hand, the anesthesia may be carried higher if the operator so desires. When the required observations have been completed, the buret is elevated so as to refill the spinal canal and wash out the anesthetic through the lumbar needle. The high effects of the anesthesia begin to disappear within four or five minutes, and sensation and movement return in the lower extremities in approximately twenty minutes. No ill effects from the procedure were noted when it was carefully carried out.

The findings confirm the observations of Foerster and indicate that chordotomy (section of the anterolateral column of the spinal cord), when successfully accomplished above the level required for complete analgesia, as shown by this test, is capable of abolishing pain and temperature permanently from the involved portion of the body.

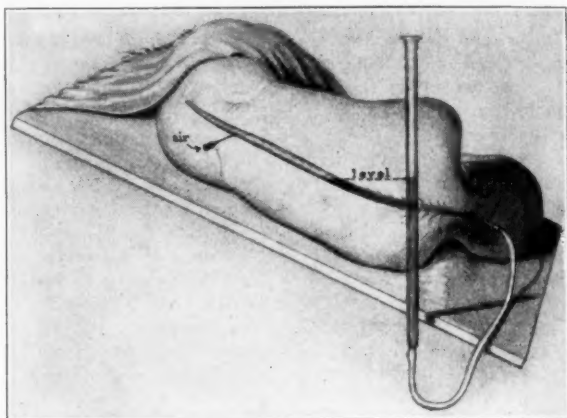
The operations devised for relief of pain by means of rhizotomy, ganglionectomy and periarterial sympathectomy may find more appropriate solution in the single operation of chordotomy when the appropriate level for this procedure has been established.

The value of the method for studying segmental pain is indicated, as well as its possible use in differential diagnosis as to the origin and existence of vague types of pain. The possible value of the method, from a purely surgical point of view, lies in the fact that a definite control of the level of anesthesia may be maintained by the operator at all times, and the residual effects due to otherwise uncontrolled diffusion are removed through the process of washing out the spinal anesthesia after its desired effects have been obtained.

## DISCUSSION

DR. TEMPLE FAY: A means of controlling the level of anesthesia and analgesia for purposes of studying various types of pain has been desired in order to establish a correct diagnosis and to initiate methods for relief of various types of intractable or vague pains, which are so frequently encountered.

The method described has the advantage of being as simple as the combined Queckenstedt test for tumors of the cord. The only risk involved is dependent



Diagrammatic representation of the method used to control the level of spinal anesthesia. Raising or lowering of the buret produces a similar change in the column of spinal fluid and in the layer of spinal anesthesia. The effects of the spinal anesthesia may therefore be arrested any desired level and ultimately washed from the spinal canal.

on the operator's skill in undertaking cisternal punctures. With this simplified method it is possible to observe the patient during attacks of pain, as to both subjective and objective responses. In two cases of "amputation neuroma" of the lower extremities, chordotomy at the fifth cervical segment produced complete loss of superficial sensation and of sensations of temperature in those parts. The patient experienced pain, however, when using the artificial stump, and pain could be produced by deep manipulation of the vessels about the area of amputation. In one case, the peripheral nerves had all been sectioned, without relief, prior to chordotomy. In another instance, spinal anesthesia raised to the level of the umbilicus (ninth thoracic dermatome) failed to remove the subjective pain, which was dull and aching and could be produced by deep manipulation of the stump. When the anesthesia was raised to the third thoracic dermatome (axillary area), the patient experienced complete subjective and objective relief, which persisted

until the effects of the anesthesia had worn off. In tabetic patients, the return of pain after chordotomy at the fifth thoracic segment has discouraged the use of chordotomy; although evidence in the light of our present analysis indicates that chordotomy was performed formerly at a level (fifth thoracic segment) probably below the point of entry of all pain fibers from the lower extremities and viscera. The test which we are presenting offers a better analysis for this and other types of clinical pictures.

DR. WILLIAM C. SPILLER: I wish to express my admiration for this ingenious method to determine the proper level of anesthesia in performing chordotomy, and to inquire whether Dr. Gotten and Dr. Fay use it in every case of chordotomy. When the test for anesthesia is made during the operation, it is not always easy to determine the ascending level of anesthesia to pin-prick and temperature from the responses of the patient, as the knife is made to penetrate deeper into the spinal cord in performing chordotomy. The mental condition of the patient at this time is not the most favorable for accurate results. To determine the necessary level of anesthesia to destroy spontaneous pain, it is well to recognize that such pain may be intermittent, and an attack may not occur while the patient is on the operating table. When abolition of pain due to pressure is the object desired, the proper level may be determined more easily.

A distinction must be made between the sensation of pressure and pain produced by pressure. In 1906, I determined that sensation of pressure in the face is not conveyed by the trigeminal nerve, as the sensation is not lost after an operation on the sensory root of the nerve in cases of *tic douloureux*, although the pressure then causes no pain. In one case in which burning pain persisted in the entire sole of the foot after chordotomy, grasping the limb firmly produced no pain in the thigh or foot. Deep pressure made with the end of a fountain pen in the thigh over the femur produced a distinct sensation of pressure but not the slightest discomfort. This finding would seem to indicate that the spontaneous burning sensation of pain was conveyed over the pain fibers which accompany the sympathetic fibers, on the arteries. Dr. Fay believes that such pain fibers are independent of the sympathetic system, and that those coming from the lower limb enter the spinal cord as high as the third thoracic roots. It is above this level that he recommends chordotomy for pain in the lower limb, and he prefers the fifth cervical segment for this purpose.

In what proportion of cases has Dr. Fay found persistence of pain after chordotomy for relief of pain in the lower limbs? I have observed it only in the case to which he has alluded, and I did not consider it a serious complication in the cases he has studied in which Dr. Frazier performed chordotomy high in the thoracic region. There was a large psychic element in the case mentioned. This patient could be relieved by capsules containing sugar; the pain was most likely to occur when he was alone with his wife, and he seldom showed the evidence of pain when he was in the company of strangers. He had suffered a fracture of the ilium with involvement of the sciatic nerve in the World War.

With what frequency has Dr. Fay seen persistence of pain after operation for true *tic douloureux*? I have not observed it. It might occur after partial section of the trigeminal root. Would Dr. Fay recommend lower cervical chordotomy for such persisting pain in the face after operation on the trigeminal nerve, or what site would he select? As he has had much experience with chordotomy, can he not determine the proper level for operation without using the ingenious instrument which he and Dr. Gotten have demonstrated, or does he regard the variation in different persons to be so great as to require the use of this instrument in every case in which he performs chordotomy?

DR. ERNEST A. SPIEGEL: As Dr. Spiller has explained, the question of pain is extremely complicated. It is generally accepted that the spinal thalamic tract carries the impulses from the opposite side. This is true for most cases. I

remember, however, a case in Vienna in which the patient had softening of the spinothalamic tract on one side of the medulla oblongata, but the conduction of pain was preserved from the other side. This case was later reported by Pappenheim. In experimentation with animals, one usually finds homolateral as well as crossed conduction of pain. After hemisection of the cord, reactions to pain can be elicited by stimulation of the crossed or of the homolateral sciatic nerve. Besides the long system for conduction of pain, there seem to be short systems, as shown by Schiff, Karplus and Kreidel, through crossed hemisections. My own experiments with stimulation of the femoral artery or of the pelvic nerve led to a similar conclusion for vascular and visceral pain. Finally, there seem to exist in certain cases not only spinal but also extraspinal conduction of pain. Dr. Spiller has pointed out that Dr. Fay came to the interesting result that impulses of pain from the viscera should reach the cord at a relatively high level. This result is perhaps a consequence of the fact that the fibers are arranged in the spinothalamic tract in such a way that the fibers from the lowest segments lie on the periphery and the fibers from the highest segments lie in the uppermost parts of the tract. One has to consider the possibility that spinal anesthesia goes into effect at least partly by a diffusion of the toxin into the spinothalamic tract, as indicated by the marginal degeneration in Spielmeier's experiments with stovaine (benzoyl-dimethylaminoethyl propanol hydrochloride). If the toxin paralyzes only the most peripheral fibers at a certain level, the resulting anesthesia should be found in lower segments than would occur if all fibers of the spinothalamic tract are mechanically severed. I hope that Dr. Fay's method will deepen knowledge, particularly of the segmental supply of visceral organs.

DR. F. C. GRANT: This method should be of value in helping determine the level at which chordotomy should be performed for relief of pain in the pelvis or lower extremities. I was particularly impressed with the statement that the authors could raise or lower the anesthetic level almost at will by washing the anesthetic material out of the cord, and that the level of anesthesia could be made to disappear in this way in twenty minutes. My opinion concurred with that of Dr. Spiegel, that the anesthetizing agent combined with the nerve cells in a manner similar to that of ether, and that it would be impossible to remove it by irrigation. However, the anesthetic material used in these experiments may act in a different manner.

My experience with chordotomy differs from that of Dr. Fay. In the clinic with which I am associated, chordotomy is now always performed at the third thoracic segment. If a bilateral chordotomy is performed, the second and fourth thoracic segments are chosen. With the possible exception of the case referred to by Dr. Spiller, in which there was great doubt as to whether the residual pain was actual or imaginary, I cannot remember any case, in an experience covering more than sixty chordotomies, both unilateral and bilateral, in which there was residual pain similar in type to that to which Dr. Fay referred. In several cases, to be sure, the original pain was not entirely relieved, owing to the fact that the incision into the cord was not of sufficient depth to bring the level of anesthesia to the required height, but I have never seen burning pain in the anesthetic area as a sequel to chordotomy. I am entirely convinced that for relief of pain in any area below the level of the ensiform cartilage, with the possible exception of the pain accompanying tabes, a properly performed chordotomy is the operation of choice.

DR. TEMPLE FAY: Dr. Spiller has referred to the sense of deep pressure, which as he pointed out in 1907, is supplied to the face by nerves other than the trigeminus. Ivy and Johnson published his views at that time. Observations on the sensation supplied to the head and neck were presented before the American Neurological Association by Dr. Spiller and me in 1926, and it was in an attempt to establish collateral sensory pathways to the face and to understand atypical facial neuralgia better that this method of spinal anesthesia was devised; my continued interest in the subject has been because of Dr. Spiller's stimulus and profound analysis.

In answer to Dr. Spiller's question as to whether or not residual pain may exist in the face after destruction of the trigeminal root, I have experienced, to my regret, in at least five cases, that following total section of the trigeminal root atypical facial neuralgia persisted, and that this residual pain was partly obliterated by subsequent stripping of carotid arteries about the bifurcation. Section of the cervical sympathetic chain below the superior ganglion apparently had no influence on this pain. My observations have been published from time to time and have led me to the conviction that pain fibers from the face may find entry into the nervous system by structures other than the trigeminus, namely, along the arterial and venous vascular tree into the thorax and thence into the lower cervical and upper thoracic cord, as well as by recurrent fibers into the sheath of the vagus nerve through the ganglion nodosum, and by some fibers which pass directly through the superior cervical ganglion to turn back into the ganglion nodosum. I have not found evidence that pain fibers pass through the cervical sympathetic chain, but have frequently demonstrated their presence in the carotid sheath (a portion of these fibers enter the vagus); other pain fibers continue along the common carotid below the bifurcation, and I have been surprised to find reference of pain under local anesthesia to the gums and face when faradic stimulation of the internal and external jugular veins was attempted.

I have not seen return of true trigeminal neuralgia after total section of the trigeminal root, and if Dr. Spiller's question refers to true trigeminal neuralgia, I believe that section of the root completely abolishes this mechanism, and that residual pain, if any, must be ascribed to another mechanism. It is important to differentiate clearly true trigeminal pain from the dull, aching, throbbing, constant type of pain which I believe to be of the vascular type, due to involvement at some point along the vascular tree. Pathologic conditions involving the vessels of the upper part of the thorax and neck, therefore, may produce a pain that is referred to the face; it is this system of pain fibers which apparently enter the upper part of the thoracic cord and perhaps the lower two cervical segments of the cord. This explains, in my opinion, why some patients find relief from pain in the head and neck when spinal anesthesia is raised to the fifth cervical segment.

Such a case was encountered not long ago, in which, following total section of the trigeminus, subjective "vascular pain" persisted. Deep pressure along the course of the facial, temporal, supra-orbital and infra-orbital vessels in the anesthetic area of the face produced pain. Spinal anesthesia raised to the fifth cervical segment brought immediate subjective and objective relief, and chordotomy at the fifth cervical segment on the opposite side has been attended with relief from this pain in the face.

I am not sure that "deep pressure sense" and "pressure pain" are similar. Certainly, deep compression over the facial, temporal, supra-orbital and infra-orbital arteries is capable of producing pain when the trigeminus, the ninth and the upper three cervical roots have been divided, giving complete superficial anesthesia of the face and neck on one side (excepting for the area of the vagus about the ear). I believe that the test will be of considerable value in certain types of atypical neuralgia and, as experience increases, chordotomy at the fifth cervical segment may replace other methods for relief of this type of pain.

I do not believe I can answer Dr. Spiller's question regarding the adoption of a fixed level for chordotomy as yet desirable for all cases. In the future, Dr. Gotten and I shall use this method for determining the level for chordotomy and perhaps, after four or five years, we can suggest an appropriate level at which the operation may be performed with maximum benefits. Dr. Spiller mentioned our former method of attempting to determine the appropriate level for section of the anterolateral column by objective testing during the operation of chordotomy itself. He has mentioned the undesirable factors and the great difficulty in obtaining proper responses at such a critical moment for the patient. The method of controlled spinal anesthesia, however, as here presented, makes it possible to perform these tests before the operation is undertaken and at a time most desirable for the patient and the clinician. The observations may be recorded, and when an element of doubt exists, the test may be repeated. The operation for chordotomy

may then be recommended at the level which the test discloses as being safely above the point of entry of all pain-conveying fibers concerned with the patient's symptoms. I believe that the operation of chordotomy, which Dr. Spiller suggested in 1907 and reported in 1912, will come into more universal application as a means for relief of pain when careful studies indicate its greater possibilities.

In reply to Dr. Grant's statement that he has not observed residual pain after chordotomy in his series, I recognize that the severe and aggravated forms of pain may be so sufficiently relieved by chordotomy as to obtain a satisfactory clinical result, but in the past residual pains were rather universally ascribed to "psychalgia" or to "neurotic" tendencies on the part of the patient, and no painstaking observations of record were made on the vascular bed and on the mechanism of residual pain, which may be involved even though a demonstrable superficial analgesia is recorded. I was not fortunate enough to obtain complete subjective and objective loss of pain in every case, even though the chordotomy was carried out to a satisfactory degree. If chordotomy were as universally successful as Dr. Grant implies, the need for ganglionectomy, periarterial stripping and supplementary operations for the relief of pain would not have come into existence. I believe that we all recognize a type of pain which chordotomy will relieve, and that there are other types for the relief of which we cannot fully decide what measures to employ. The test which we presented may help to determine the desirable method or at least to indicate a level for chordotomy sufficiently high to include all fibers from the involved area.

Dr. Spiegel presents an interesting consideration. I have not been impressed with the possibility that intersegmental communicating pathways for pain can explain the residual manifestations following chordotomy. That they cannot is evidenced by experimental work. I am more inclined to accept Foerster's view that these pathways for pain, passing parallel to the cord through the sympathetic chain and ganglia, enter by posterior roots at levels higher than is indicated by the pattern of peripheral nerves and nerve roots. I doubt whether such intersegmental pathways exist outside the spinothalamic tract at the level of the medulla (excluding fibers from the fifth, ninth and tenth cranial nerves). If section of the pathways for pain could be accomplished at this point, or even in the high cervical area, the majority of pain fibers from the opposite side of the body could be permanently interrupted.

I believe that the problem of pain requires careful reanalysis; the clinical methods at one's disposal may offer an opportunity of wider observation, so that many controversial points may be cleared up, as additional information is acquired through controlled methods of interrupting the pathways for pain. The method which Dr. Gotten and I demonstrated offers a variety of possibilities for clinical study, the results of which will have to await a large number of cases and continued analysis.

DR. NICHOLAS GOTTEN: I will add only that the complaint of pain following chordotomy is extremely important. Some surgeons call it psychic, and others agree with the patient that it is real. Certainly there are patients in whom there has been no evidence of psychoneurosis prior to operation who after chordotomy still complain of burning pain. I recollect well one case of this type at the Neurological Institute.

## CHICAGO NEUROLOGICAL SOCIETY

*Regular Meeting, Dec. 15, 1932*

PERCIVAL BAILEY, M.D., *President, in the Chair*

MERALGIA PARAESTHETICA. PRESENTATION OF A CASE. DR. THEODORE T. STONE.

*History.*—I. T. N., a physician, aged 28, was well until March 1, 1932, when, on arriving in California from Chicago, he had severe allergic rhinitis, which

persisted during the eight months of his stay there. During the last two months that he was in California he began to have asthmatic attacks, which came on only at night and were accompanied by a severe cough which was relieved by hypodermic injections of epinephrine hydrochloride. Almost coincidentally with the onset of the asthma, an area of recurring paresthesia developed over the outer aspect of the left hip. The paresthesias appeared suddenly, lasted for a few hours, never more than twelve, and disappeared spontaneously. At times there was a feeling of numbness, with diminished sensibility to pin prick, heat, cold and touch. At other times there was increased sensibility to pin prick, heat and cold; for example, a lukewarm hand placed on the thigh felt red hot, and a cool hand seemed like ice. Contact with bed sheets and clothing seemed to irritate the area. The symptoms disappeared spontaneously about a month after the onset.

The patient returned to Chicago on Nov. 1, 1932; on his departure from California, the allergic symptoms disappeared.

About ten days ago the paresthesias returned and had the following distribution: the outer aspect of both hips and the inner surface of both thighs. They persisted for forty-eight hours in the right hip and for twenty-four hours in the left thigh. The sensations disappeared spontaneously. Two days ago the symptoms returned, but only over the left hip; they were mild. At no time, with the exception of the allergic phenomena, has the patient had any other accompanying symptoms. He has complained, however, of having "lost pep" since the onset of the allergic symptoms.

The past history is of no moment except that, prior to the onset of the paresthesias, the patient wore tight shorts, which he believes may have been responsible for the sensations. He had bilateral lobar pneumonia in 1924. He drinks alcoholic spirits only occasionally and moderately. There is no history of injury, and the family history is without significance.

*Examination.*—There is no objective evidence of organic disease of the central nervous system, except hyperesthesia on the anterolateral aspects of the upper third of both thighs. In the center of these hyperesthetic regions are hypo-algesia and diminished sensibility to touch, vibration and temperature. The left thigh is more involved than the right. There is a positive Patrick test on the left side. All deep and superficial reflexes are normal.

A study of the blood revealed: red cells, 4,700,000; white cells, 12,200, with a normal differential count. The Wassermann and Kahn reactions were negative; the blood sugar was 84 mg. per hundred cubic centimeters, and the blood non-protein nitrogen was 28 mg. Roentgenograms of the teeth and the lumbosacral spine show normal conditions.

*Comment.*—Meralgia paraesthetica is an uncommon but clearly defined acute clinical condition involving the lateral femoral (external) cutaneous nerve. It is characterized by paresthesias, hypo-algesia and pain over the outer or anterolateral aspect of the thigh. This nerve is entirely sensory and is derived from the second, third and fourth lumbar roots. The condition occurs in men more often than in women. It may be unilateral or bilateral. The pain and paresthesias are most marked on standing and walking. The symptoms may come and go (paroxysms). In most cases one finds hypo-algesia and diminished sensibility to all forms of stimuli. Hyperesthesia may be present around the hypo-algesic area.

The condition is caused essentially by involvement of the lateral cutaneous nerve in its periphery. The symptoms are not to be confused with subjective or objective evidences of the involvement of this nerve by a central lesion, such as tabes, tumor of the cord, spondylitis, syringomyelia, osteoarthritis, meningomyelitis or arachnoiditis. The condition is a neuritis due to direct trauma, abnormal posture, infections, excessive standing, pressure on the fascia lata of the thigh, obesity, gout or pressure from parts of the clothing, especially from waist belts. The infections include syphilis, typhoid and acute articular rheumatism. Alcoholism and diabetes may produce the symptom complex.

Pathologic examination in one case by Nawratzki revealed neuritis and perineuritis, with marked atrophy of the nerve fibers.

Treatment should be conservative, with the use of antineuralgic drugs, electrotherapy and hydrotherapy. If the condition becomes intractable, one may divide or resect the external lateral cutaneous nerve peripherally or slit the fascia lata that compresses it. Injection of alcohol is difficult because of the depth of the nerve.

The condition is known as meralgia paraesthetica of Roth or Bernhardt's disease.

#### DISCUSSION

DR. ALBERT B. YUDELSON: About four years ago I saw a man with hyperesthesia and hypo-algesia in the distribution of this nerve on the left side. The symptoms had recurred for three years in succession regardless of the season of the year. In the fall of 1931 hyperesthesia appeared, and the pain was more excessive. Two months later, in the early part of December, herpes zoster appeared over the area that had previously been hyperesthetic. The condition cleared up after the patient had rested in bed for nearly two months.

DR. GEORGE W. HALL: I discussed a case of this type with Dr. Patrick; he believed that the symptoms would disappear with the use of the faradic brush.

DR. ROY GRINKER: How does Dr. Stone explain the distribution of the sensory symptoms on the inner surfaces of the thighs, the paroxysmal nature and the bilateral territory, if this is meralgia paraesthetica?

DR. THEODORE T. STONE: The description of meralgia paraesthetica in the literature shows misunderstanding as to the term. Any condition of hyperesthesia and hypo-algesia may be diagnosed as meralgia paraesthetica. Roth, in 1929, stated that meralgia paraesthetica in an involvement of the external lateral femoral sensory nerve alone. The genitocrural nerve may be involved similarly. One can explain the sensory loss only by changes in the sensory nerve. I do not know whether the cause is a neuritis, an edema of the nerve sheath or some other process. Neuritis of various types is characterized by periodic attacks. This is true not only of neuritis or neuralgia without pathologic changes, but of the ordinary forms of infectious neuritis. If the nerve is examined, one may find definite evidence of inflammation of the sheath or of the nerve itself.

#### ABNORMALITY OF THE CERVICAL SPINE WITH MIRROR MOVEMENTS. DR. LOREN WILLIAM AVERY (by invitation).

*History.*—The patient suffered no injury at birth, and has no familial or inherited tendencies toward spinal abnormality. At birth there was a tumor in the occipital region in the midline. Eighteen months later the tumor was removed. It was about the size of a walnut, but I have no data as to its character. As long as the patient can remember, he has had disturbances involving the movements of the fingers, which are practically limited to the execution of delicate actions, such as buttoning the clothes, tying ties and handling table implements. There is no disability for movements of the hands, though they are not absolutely accurate. Even as a child he was able to throw a football or a baseball with ease.

Accompanying the disturbance mentioned is the phenomenon to which has been given the name of mirror movements. These are abnormal, associated movements in the hands and toes. Movements which the patient makes with the fingers of one hand in the attempt to do anything are practically duplicated in the fingers of the opposite hand. The same statement may be made with respect to the feet, though here the duplication is not so striking and can be overcome. The mirror movements are present not only in voluntary actions; in passive movements of the hands or fingers the same phenomenon occurs. The patient has also had a disturbance of the eyes from the time of his earliest recollection; he readily sees double in the vertical plane, though not from side to side. He has no difficulty in bringing the two images together. He did not wear glasses as a child.

There has been a steady improvement as he has grown older; he can now dress himself satisfactorily, though he needs the aid of a buttonhook to fasten his collar.

He is able to write and to draw; he has done considerable mechanical drawing which is above reproach.

*Examination.*—The pupils are slightly irregular, but within physiologic limits. On closer observation, it is seen that the right eye is directed slightly higher than the left. The neck is not extremely short; the patient has good movement of the neck, with no limitation. He has movements at all joints of the extremities. The movements are strong and, with the exception of those of the hands and fingers, are executed with good synergy. There is distinct adiadokokinesis in the hands.

The hand is of good contour, does not show atrophy and is well developed. There is a tendency to overextension of the fingers, as well as a suggestion of contracture of the little finger in flexion. Movements of the fingers are extremely awkward. The patient has great difficulty in handling small objects. There is distinct astereognosis, with slight disturbances of joint, tendon and touch sensation. The ability to use the fingers is much less in the dark or when the patient is not watching them. He is able to execute all movements of the fingers to a certain degree, though he separates them and brings them together again apparently largely by the long extensors and flexors.

The electrical responses are good in all the muscles except the interossei. The tendon reflexes are normal. There are no pathologic plantar responses nor any marked Romberg sign.

Roentgenograms show a disturbance of the cervical spine. The third and fourth vertebrae are fused. There is a normal intervertebral space between the seventh cervical and the first dorsal segment, the remaining spaces being rudimentary. No spina bifida is apparent.

#### OPHTHALMIC CHANGES PRODUCED BY PRECHIASMAL AND CHIASMAL LESIONS.

DR. W. I. LILLIE, Rochester, Minn. (by invitation).

Tumor of the brain is relatively rare. Yet disturbance of the special senses, mentality, motion, speech, sensation, equilibration, metabolism and growth and the development of various dyscrinisms and of symptoms such as pain in the head and convulsions are frequent. Therefore the consideration of tumors of the brain in differential diagnosis is common, especially if the phenomena mentioned are insidious and progressive.

Tumors of the brain are neither precise nor consistent in the phenomena they produce. The great variations in the biodynamic characteristics of tumors, as exemplified by the mode of progress, the rate of growth and the direction of extension, bring about sequential relationships of almost infinite diversity.

Examination of the eyes affords significant data both in the diagnosis and in the localization of tumors of the brain. As this consideration presumes the integrity of the end-organ, it is the duty of the ophthalmologist to correlate any local pathologic condition of the eye with an appropriate alteration in vision and in the visual fields.

Headache, vomiting and choked disks are the classic combination indicative of tumor of the brain. But this symptom complex may appear only in part, or may be entirely absent even in a case which presents such steady deterioration of a localized cerebral function that the assumption of the presence of a tumor of the brain is almost imperative. Not infrequently in cases of prolonged illness with vague symptoms, pronounced choking of the disks suddenly develops as the first significant clue. Gradually progressive blindness that is explained by the secondary consequences of long-standing choked disks is more serious still. Rational management requires repeated observations of the fundus under a great variety of presenting symptoms. The same statement may be made with respect to pallor of the disks and the simple optic atrophy seen with lesions about the chiasm and the optic nerve. The visual acuity and the extent of the fields furnish a precise measure of the functional integrity of the visual system. The importance of data so obtained in the diagnosis and in the localization of tumors of the brain has been well established by many investigators.

The accurate elicitation of fields is the work of those especially trained in the physiology of vision and in the use of suitable apparatus. However, any physician may familiarize himself with the technic of diagramming the fields, using his own visual fields as a measure of those of his patient. He can thereby acquire sufficiently accurate data for the detection of gross defects or for guidance in making more detailed studies.

In the presence of a tumor of the brain, normal visual fields are also significant, justifying the presumption that the site of the growth is to some degree remote from the visual pathways.

The visual fields may furnish the only signs of value in localizing a tumor. Especially is this true in the presence of a chiasmal or a basal frontal tumor.

*Basofrontal Group.*—Lesions involving the basal portion of the frontal lobe or arising in the olfactory groove produce a definite ophthalmologic syndrome. The Gowers-Paton-Kennedy syndrome is optic atrophy and scotoma on the side of the lesion, with choked disk in the other eye. Several combinations of signs may occur: (1) unilateral central scotoma with a normal fundus; (2) unilateral central scotoma and pallor of the disk; (3) bilateral central scotoma with pallor of both disks; (4) bilateral central scotoma with choked disks in both eyes; (5) unilateral amaurosis with simple optic atrophy, and choked disk in the opposite eye; (6) unilateral amaurosis with simple optic atrophy, and choked disk and central scotoma in the opposite eye; (7) central scotoma and various alterations of the peripheral fields caused by secondary contraction resulting from choked disks, and (8) bilateral amaurosis with any of the aforementioned changes in the fundus.

Such variations in the ocular signs are indicative of the various influences to which the optic nerves are subjected and also of the associated influence of the choked disks. In certain cases the situation of the tumor may be such as to affect the chiasm by extension, thus adding further changes in the field. If the evolution of the ocular changes can be studied repeatedly, the data furnished should permit an accurate estimation of the site and the rate and mode of extension of the lesion. The steady evolution of these signs is the main support of the diagnosis of tumor, as distinguished from other conditions which produce some of the signs mentioned, especially scotoma and simple optic atrophy such as are seen in multiple sclerosis, basilar gummatous meningitis and other inflammatory lesions. Inflammatory conditions usually have a rapid onset, are progressive for a short time and then regress noticeably, regardless of the type of treatment employed; thus they are distinguished from the slowly progressive syndrome generally produced by a tumor.

Basilar gummatous meningitis and chronic local arachnoiditis usually produce a slowly progressive syndrome relating to the prechiasmal and chiasmal region. The former can be diagnosed readily by the serologic and cytologic changes in the cerebrospinal fluid and needs no further consideration here.

*Chiasmal Group.*—The ocular syndromes produced by lesions at or near the optic chiasm have been well classified by Cushing, who enumerated seven possible causes: (1) meningiomas with a parasellar, rather than a suprasellar, point of origin; (2) pituitary adenomas; (3) congenital tumors arising from the cranio-pharyngeal pouch; (4) gliomas arising from the chiasm or the third ventricle; (5) chronic local arachnoiditis; (6) syphilitic meningitis, and (7) aneurysms. Any one of these may affect the optic nerves, chiasm and either or both optic tracts in varied combinations, producing definite ophthalmic changes. The usual changes are summarized as: (1) lowered central visual acuity; (2) pale optic disks or simple optic atrophy; (3) bitemporal hemianopia for colors; (4) bilateral hemianopia for form and colors; (5) bitemporal scotomatous hemianopia for colors or form or both; (6) temporal hemianopia with amaurosis of the opposite side; (7) temporal hemianopia with successive changes which lead to amaurosis, such as central scotoma, cecentral scotoma and enlargement of the scotoma, with islets of vision and amaurosis; (8) homonymous hemianopic scotoma for form and colors; (9) homonymous hemianopia for colors, and (10) homonymous hemianopia for form and colors.

A significant feature of the defects in the visual field produced by chiasmal lesions is the asymmetry, whether bitemporal or homonymous, in contrast to the symmetrical defects produced by lesions affecting the optic tracts or radiations.

When a pituitary tumor is suspected, and roentgenograms show enlargement of the sella turcica, while clinically there are signs of hypophyseal dysfunction, it is nearly always possible to make a preoperative diagnosis. Cysts of the cranio-pharyngeal pouch usually manifest themselves relatively early in life, and roentgenograms show shadows cast by calcium deposits in the wall of the cyst. Gliomas of the optic chiasm have been found to occur with relative rarity and often are associated with anterior pouching of the sella turcica, as revealed by roentgenograms. Aneurysms around the optic chiasm seldom have an audible bruit and sometimes present difficulties in differential diagnosis, although the roentgenogram is often pathognomonic. Suprasellar meningiomas generally indicate their presence only by impairment of vision; the fields become bitemporally constricted, although, as a rule, the process does not advance with equal steps in both eyes, and a roentgenogram of the sella turcica shows a normal condition. Generally, there is little or no hypophyseal dysfunction associated with this group.

In a certain percentage of cases in which symptoms of a chiasmal lesion are present it is impossible to predicate the underlying lesion. Further, patients who fail to respond to conservative methods of treatment for this condition are faced with a grave prognosis unless radical measures are adopted. Certain chiasmal lesions which simulate pituitary disorders do not reveal evidence of a neoplasm at operation; often a definite inflammatory condition involving the region of the optic chiasm is disclosed; the optic nerves may be found covered with an inflammatory exudate and bound down in a mass of adhesions. Tumefaction of the inflammatory exudate, which consists of encysted fluid, may also be present. By freeing the adhesions with a blunt hook and allowing the escape of the encysted fluid, it is possible to check the progress of the condition or to alleviate the symptoms.

In my experience, patients in whom the optic disks were normal in appearance or who had pallor of the disks without loss of substance, obtained the greatest gain in visual acuity and extent of the visual fields following surgical intervention. In practically all cases the scotomatous field changes were at one time or another continuous with the physiologic blind spot, and the blind spot was almost always incorporated in the temporal field defect, either for form or for color. The presence or absence of color field defects was as important as the presence or absence of form defects. Roentgenograms of the sella turcica showed normal conditions in a higher percentage of cases of intracranial lesions not of pituitary origin than of those of pituitary origin.

Any person suspected of having an intracranial lesion affecting the chiasm should have a thorough nasopharyngeal examination. The origin of lesions affecting the chiasm cannot be definitely determined from ophthalmologic examination.

#### DISCUSSION

DR. PERCIVAL BAILEY: These patients do not always come to the neurosurgeon late because the ophthalmologist has not been alert. I recently operated on a patient who was seen by Dr. Lillie a year ago; he advised operation, which was refused. The patient came to me six months ago, and I advised operation; she came back again when vision was entirely lost in one eye and reduced in the other. Many ophthalmologists detect these troubles early.

It is important not to discuss intracranial tumors as though they were all alike. They must be differentiated from a pathologic standpoint as well as from that of localization. Unilateral central scotoma, either alone or with adjacent abnormalities, is associated almost always with meningioma in the olfactory region, and the ophthalmologist alone is thus able to make a pathologic diagnosis. I was interested to hear that he no longer tries to make a pathologic diagnosis of tumors in the neighborhood of the chiasm. While it is true that one cannot do this so well as in the case of an olfactory tumor, I believe that it is possible to derive

some idea as to the pathologic nature of a chiasmal tumor from the ophthalmic findings. In my experience, the patient with a suprasellar tumor or cyst is more likely to present a central scotoma early and a peripheral defect late, whereas with the patient who has an adenoma the reverse is true.

In the case of a tumor in the chiasmal region, there are other means of making a diagnosis. When one takes all the data and puts them together, a pathologic diagnosis is usually possible.

Dr. Lillie thinks that qualitative perimetry is more accurate than quantitative, but he also employs quantitative methods when he uses smaller test objects than most ophthalmologists do. I agree with him on the last two points. One ophthalmologist at our clinic thought that he could distinguish tumors of the posterior fossa and others by the appearance of the fundus, but I think he has given that up; I have never known typical binasal defects to occur with cerebral tumors until atrophy begins.

DR. GEORGE W. HALL: I was interested that Dr. Lillie believes that the presence of a central scotoma, plus an increased cell count in the spinal fluid, is sufficient grounds for a diagnosis of multiple sclerosis. I understood him to say that he did not think the sinuses were of much importance as an etiologic factor. One or two years ago, in a discussion before the Ophthalmological Society, some of those present thought that the sinuses played a large part as an etiologic factor in multiple sclerosis. If ophthalmologists would concern themselves more about the early findings in multiple sclerosis, this process could be checked in many cases, and fewer patients would present the typical symptoms we see so frequently in the hospitals. I agree with him that one cannot wait until the classic picture found in the textbooks develops if one desires improvement under modern methods of therapy.

DR. LEO MAYER: I think that the emphasis which Dr. Lillie has placed on an examination of the fields with small objects is important. Ophthalmologists today are doing far more in this respect, using methods that will show changes much earlier. Another point is that the ophthalmologist cannot always diagnose the type of lesion; he can merely say that a lesion of a certain type is suspected. These two points are important for the neurologist to know when he consults with the ophthalmologist.

DR. W. I. LILLIE: Quantitative perimetry should be combined with qualitative perimetry. Visual defects are much more readily demonstrated by the presentation of colors than by that of minute objects. Although examination of the visual fields is not a scientific procedure, nevertheless a qualified examiner should have a basic knowledge of cerebral anatomy and physiology. The relegating of the examination of the visual fields to the girl employed to tend the office is an abominable procedure and probably accounts for the frequent failure in proper localization of the lesion. What neurologist would accept the sensory findings charted by such an employee or a nurse in the localization of a lesion of the spinal cord? Diagramming the visual fields should be to the ophthalmologist an analogous procedure.

The ophthalmologist cannot predicate definitely the type of lesion producing the ocular changes, but in a large percentage of cases, if the associated structural changes and history are correlated, the syndrome is more or less pathognomonic.

Any of the syndromes can be produced by an inflammatory, vascular or neoplastic lesion. The course of events will usually suffice to separate the etiologic factor. Retrobulbar neuritis, whether due to multiple sclerosis, nicotine, alcohol, heavy metals or other causes, may simulate a basofrontal lesion and must be excluded before an intracranial operation is performed. My experience as to retrobulbar neuritis being caused by sinusitis is on the negative rather than on the positive side. Over 60 per cent of the patients I have seen with prechiasmal and chiasmal tumors had had sinus operations before intracranial surgical intervention was instituted.

## Book Reviews

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**Correction of Defective Speech: A Complete Manual of Psycho-Physiological Technique for the Treatment and Correction of the Defects of Speech.** By Edwin B. Twitmyer and Yale S. Nathanson. Price, \$3.50. Pp. 450. Philadelphia: P. Blakiston's Son & Co., 1932.

This book is dedicated to the proposition that "the ability to communicate with fellow human beings by means of articulate language is an inalienable right." Any deprivation of this right leads to a distortion of the personality and an interference with the normal economic and social development of the individual. This affects not only the individual, but, as it is impossible to separate the individual from the group, the latter must suffer as well. Consequently it is of utmost importance to devise a method of treatment by which those suffering from any of the various defects of speech may be restored to their inalienable right. The authors have kept this purpose in mind while preparing this manual for a psycho-physiologic treatment of speech defects.

In most cases of speech defects the prognosis is good, provided the proper approach is made in each case. In general, such an approach should consist of three parts. First, the patient should have thorough medical care, with proper examinations and treatment to restore him to the best possible physical condition. Then he should have a complete psychologic examination, including an analysis of his mental and emotional states, with a view to giving him integration of his mental processes and a desire for normal speech. Finally, he should be given a course in speech training to develop the proper processes of articulation.

It is with this third part of the approach that the book primarily deals. For normal speech there are three essentials: first, correct breathing; second, the correct kinesthetic or muscular imagery, called by the authors the "orotans," and finally, the proper combination of these two to produce normal articulation. With these points in view the authors have prepared a series of exercises to cover breathing, orotans and their coordination. To prepare such a series of exercises, especially in the case of those which aim to develop a proper orotans for each of the various sounds, it is essential that these sounds be analyzed and that their mode of formation be determined. Consequently it is necessary to have some classification that will be based on the manner of formation of the respective sounds. Speech consists of "continuants," which are commonly spoken of as the vowels, and "stops," which are consonants. The latter are divided into groups and classified according to their manner of formation, e. g., as dentals, labials, etc. Each of these groups is covered by exercises which illustrate the proper orotans for the particular consonants when appearing either alone or in combination with vowels and other consonants. The exercises are graded so that the patient studies the groups one at a time, with the material of each exercise so arranged that he passes to the unknown from the known. Thereby he gains confidence in his own ability, a factor of paramount importance in handling any speech disorder.

In addition to these exercises, the book contains material that should be of use to any one engaged in speech correction. In the foreword there is an interesting discussion of the relation of the individual to his environment. In part I are some statistics on the frequency of words and the relative percentages of the various sound groups occurring in these words. Part III describes a case record, the use of which the authors have found to be not only stimulating to the patient, but beneficial to the instructor as well. In the addenda, Dr. Nathanson discusses a "'Conceptual' Basis of Habit Formation," and gives a method of treating certain of the "unconscious habits."

For those speech defects in which the difficulty is with articulation, the exercises and the manner of approach advocated should be decidedly beneficial. On the

other hand, in cases of stammering, in which the difficulty is largely psychologic, such speech exercises may be not only useless, but harmful. The authors have taken a commendably sane attitude, however, by saying that each case is a case unto itself, and that while the various schools for speech correction are by no means all wrong, nevertheless not one of them can offer a panacea.

**The Heart Rate.** By E. P. Boas and E. F. Goldschmidt. Price, \$3.50. Pp. 166. Springfield, Ill.: Charles C. Thomas, 1932.

In 1928, Boas described the cardi tachometer, an apparatus designed to count automatically and record the heart rate for prolonged periods of time. Using this instrument, Boas and Goldschmidt report studies based on continuous records over periods of from twelve to forty-eight hours on 356 persons. The heart rate was studied during sleep, during the normal activities of the day, during anesthesia and operations and in certain diseases, particularly cardiac insufficiency, exophthalmic goiter and neurogenic sinus tachycardia. Almost one third of the book is devoted to a study of the heart rate during sleep.

In an attempt to establish normal values for healthy men and women, respectively, the authors computed the minimum, maximum, average and basal rates. The basal rate was the rate recorded early in the morning, shortly after the subject awakened and before arising. The average heart rates in the sleeping and waking states demonstrate clearly the marked slowing of the heart during sleep. The rate during sleep was approximately 20 per cent less than the average rate during waking hours, and the minimum rate during sleep was approximately 15 per cent lower than the basal heart rate. They believe that the slowing of the heart during sleep results from the following causes: decreased muscular and mental activity, decreased reflex excitability, lowered body temperature, lowered basal metabolism and increased vagal activity due to the influence of the hypothetic regulating center in the hypothalamus.

Study of the heart rate during the normal activities of the day revealed some unsuspected data. The routine morning toilet was accompanied by a cardiac rate of from 100 to 118 in almost every subject. Dancing produced a much greater acceleration of the heart than one would expect. After mild exercise the rate returned to normal in a few minutes or less, while after heavy work it is most significant that the pulse usually remained elevated for many hours, frequently persisting during the sleep of the subsequent night. In those accustomed to tobacco no effect on the heart rate was observed during smoking. One record was obtained on a man and wife during sexual intercourse: The heart rate of the man was 143 and that of the woman 146 at the time of orgasm. It is obvious that these observations are of great importance in the management of patients with cardiac incompetence.

Study of the heart rate during anesthesia and operations confirmed the excessive tachycardias that are known to occur during subtotal thyroidectomy, prostatectomy and craniotomy. Of clinical importance is the remarkable uniformity of the heart rate during the course of operations under local anesthesia, and equally significant is the marked tachycardia before operation, especially in persons of nervous temperament, particularly if the anesthetic is started in the operating room. Another argument in favor of Crile's anoci association!

Study of the heart rate in those suffering from cardiac insufficiency showed that the tachycardia persisted during sleep. Even in coronary disease, in which the rate may be relatively slow, the customary drop during sleep was lacking. The tachycardia of exophthalmic goiter persisted during sleep, except for the partial reduction in rate that resulted from the abolition of reflex excitation by way of the unstable sympathetics. In neurogenic sinus tachycardia the heart rate during sleep was normal.

It is therefore obvious that a continuous record of the heart rate during sleep will enable the clinician to distinguish between tachycardias of organic and functional origin, and although the method is at present too cumbersome for clinical

use this study is of real and practical value. It establishes certain normal standards and points out various ways in which the knowledge of the heart rate over prolonged periods of time can be utilized in diagnosis and treatment.

**Treatment of Syphilis.** By Jay F. Schamberg, M.D., and Carroll S. Wright, M.D. Price, \$8. Pp. 658. New York: D. Appleton and Company, 1932.

This is a timely book. The authors have not only had wide experience in treatment of various types of syphilis, but can also speak from experience gained from research on the chemical aspect of preparations used in the treatment of the disease. In the first part of the book there is a general and a specific discussion of different drugs that have been used, such as mercury, bismuth, arsenobenzenes (arsphenamine and its derivatives), iodides and other metals. For example, in the discussion of the effects of arsenicals the chemotherapy, toxicity, excretion, technic of administration, various reactions, normal and abnormal, and complications are adequately presented. This is followed by a chapter on the prophylaxis of syphilis, its early and late treatment; then follow special chapters on the treatment of ocular, aural and skeletal syphilis; neurosyphilis; syphilis of pregnancy and congenital syphilis; syphilis in marriage, and last, a miscellaneous chapter on the Wassermann reactions.

Neurologists will be interested chiefly in the discussion of neurosyphilis, which takes up about seventy-five pages and is divided into three chapters. In the first are a general discussion of the problem and a discussion of the pathology, incidence and prognosis in various types. The second chapter presents spinal, cisternal and intraventricular puncture, with the technic and their indications. The third chapter discusses treatment. Particular attention is paid to tabes dorsalis and dementia paralytica. The discussion in this section is adequate; the literature is well covered, and the presentation is safe and sound.

While nothing but praise can be given for the presentation of this important subject, nevertheless, from neurologic and psychiatric standpoints, the tendency for syphilologists to treat syphilis in which the nervous system is implicated is questionable. It would be impossible for a syphilologist to be a competent neurologist, gynecologist, surgeon and so on. If the syphilologist treats such patients with the advice of a neurologist all is well, but that is not the case. Most syphilologists, because they are specialists in this line, consider themselves amply able to pass on the necessity and the type of treatment that should be used, with the consequence that in many instances patients are treated for syphilis who never have had it, or are inadequately treated or overtreated, so that the patients get the worst of it. The time has come when the neurologist and psychiatrist should treat his own patients, or they should be treated under his direction. That such is not the case today is the fault of the neurologist and psychiatrist, for he has allowed such specialists to take these patients from him.

**La folie de Vincent van Gogh.** By Victor Doiteau and Edgar Leroy. Collection "Sous le signe de Saturne." Price, 60 francs. Pp. 137. Paris: Édition aesculape, 1928.

Although the biographic study of outstanding persons from the point of view of psychiatry—spoken of as the writing of pathographies—is encountered most frequently in the German psychiatric literature, it originated in France. This account of the life of Vincent van Gogh is an excellent example of this type of work. In psychoanalytic studies in this field, and also in the older psychiatric pathographies, it often happens that the psychiatrist goes too far in viewing the eminent personalities studied—and their works—through the spectacles of scientific classifications and preconceived conceptions. This study of the life and psychosis of the eminent painter van Gogh is free from such drawbacks. A full account is given of the life and the illness of this painter, who was undoubtedly one of the greatest innovators of modern painting. The narrative is well documented by quotations from letters and conversations with people who knew

him, by his own personal letters and notes and by charts and commitment papers from the hospitals where he was treated.

In the second part of the book is a critical discussion of the nature of van Gogh's disease. The authors, whose study is far more penetrating than that of Jaspers, disagree with Jaspers' opinion that van Gogh suffered from schizophrenia. In their opinion he had an epileptoid psychosis. Their diagnosis is based on the study of hereditary factors, personal history, prepsychotic personality and the symptoms of the illness itself. The reviewer believes that the diagnosis of epileptoid psychosis is well justified by the data known about this unhappy genius. The book is well written and is clear both in structure and in reasoning. There are a number of well selected and beautifully printed reproductions of van Gogh's paintings. It deserves to be read by all interested in either art or psychiatry. To those who are interested in both, it should be exceedingly worth while. It is recommended especially to the too numerous modern psychopathologists whose first question when they approach the study of a "great abnormal," such as van Gogh, is concerned with some psychoanalytic delving into his infantile sexuality.

**Acromegaly.** By F. R. B. Atkinson, M.D. With a foreword by Sir Arthur Keith. Price, 21 shillings. Pp. 260. London: John Bale Sons & Danielsson, Ltd., 1932.

In the foreword of this interesting book Sir Arthur Keith, who has contributed to knowledge of pituitary function, comments on the niggardly recognition that is afforded to the compilers of the knowledge and emphasizes the fact that in this treatise the author has given years of toil to the systematic presentation of 1,319 cases of acromegaly. With this point of view the reviewer is in hearty accord. All so-called new discoveries are not always new or of merit, whereas, on the other hand, the compilation of useful data by a competent observer is always worth while.

Since Marie's original description of acromegaly, two monographs have appeared, the first by Professor Sternberg, in 1897, which was translated by the author of this book, and the second by Professor Messedaglia, in 1908. The 1,319 cases from the literature were collected up to the end of 1930.

The presentation of this material is short and concise, and the subject is presented in an orderly manner. Perhaps the most interesting parts of the book are the tables. The first presents the results of the removal of the pituitary gland in 77 cases; the second, an analysis of postmortem examinations in 265 cases; the third, the ocular conditions in 914 cases, and last, the description of the 1,319 cases, including the sex, age, condition of the thyroid, vertebral column, presence of albumin and sugar, condition of the tongue and general observations. Last, there is a valuable bibliography.

**Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic Nervous System.** By Harvey Cushing. Price, \$5. Pp. 234. Springfield, Ill.: Charles C. Thomas, 1932.

The contents of this volume consist of four lectures: I. "Neurohypophyseal Mechanisms from a Clinical Standpoint"; II. "Posterior-Pituitary Hormone and Parasympathetic Apparatus"; III. "The Basophil Adenomas of the Pituitary Body and Their Clinical Manifestations (Pituitary Basophilism)"; IV. "Peptic Ulcer and the Interbrain." The fourth attempts to show that there is a neurogenic cause for acute perforative lesions affecting the esophagus, stomach and duodenum in the interbrain, where, in recent years, the cerebral centers for vegetative impulses have been placed. The evidence is not altogether convincing, but with the data at hand such an interpretation should be considered for what it is worth.

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